Synthesis of Enantiomerically-Pure and Racemic Benzyl-Tethered Ru (II)/TsDPEN Complexes by Direct Arene Substitution; Further Complexes and Applications.

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Abstract

The use of a direct arene-exchange method for the synthesis of benzyl-tethered arene/Ru/TsDPEN complexes for use in asymmetric transfer hydrogenation is reported. A series of complexes tethered through a three-carbon linear chain was also prepared. The arene-exchange approach significantly simplifies the synthetic approach to this class of catalyst and permits the ready formation of modified analogues. The approach also provides a route to racemic catalysts for use in general reductions with either hydrogen or transfer hydrogenation.

Introduction.

Tethered Ru/TsDPEN catalysts, typified by complex **1** which we first reported in 2005,[1] are derivatives of the widely used Noyori-Ikariya catalysts **2** commonly used in asymmetric hydrogenation (AH) and asymmetric transfer hydrogenation (ATH) of ketones and imines.[2] The high levels of catalytic activity and versatility exhibited by the tethered catalysts **1** is likely to be, at least in part, the result of the high stability of these complexes due to the three-point attachment of the ligand to the ruthenium.[3] Several synthetic applications of the tethered catalysts have now been reported,[1,4] including industrial applications to, for example, pharmaceutical targets. Closely related complexes, such as DENEB **3**[5] and sulfamoyl derivatives **4**,[6] which were reported after our initial publications on tethered catalysts for reductions, have also been used in a number of synthetic transformations (Figure 1).

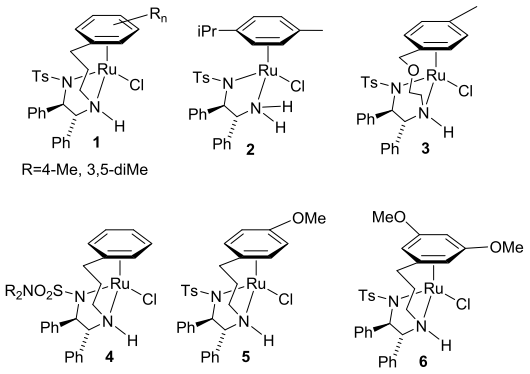
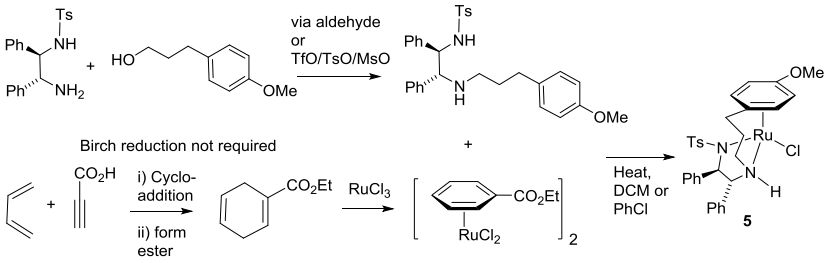


Figure 1. Tethered and non-tethered complexes for asymmetric transfer hydrogenation (ATH) of ketones and imines (*R,R*)-enantiomers illustrated throughout. Complexes **5** and **6** were prepared through an arene-exchange strategy.

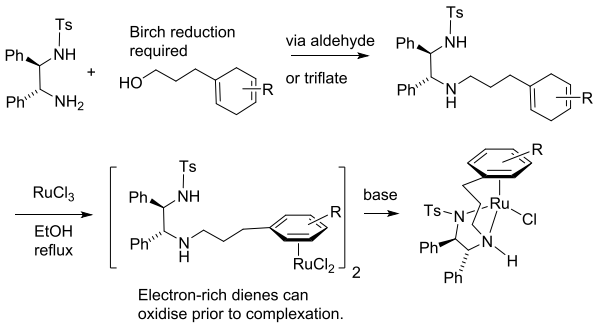
In 2013, we reported the first examples of the direct synthesis of tethered TsDPEN complexes through the use of an 'arene-substitution' process in which a more electron-rich aromatic ring on the new ligand replaced a less electron-rich one on a dimeric Ru (II) precursor (Scheme 1).[7] Prior to our report, we were aware of only two examples of related substitutions within Ru (II) arene complexes, both of which contained simple 3-carbon tethers to a single amine group.[8] This is in sharp contrast to arene-exchange reactions in complexes based on phosphines, of which numerous examples exist.[9]



Scheme 1. Approach to tethered Ru (II) complexes *via* arene-substitution.

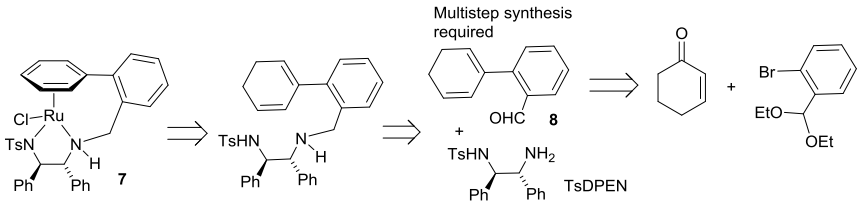
The arene-substitution route offers potential advantages over the longer-established approach in which a cyclohexadiene precursor ligand is reacted with ruthenium trichloride (Scheme 2). Specifically; 1) there is no requirement to carry out a Birch reduction; the precursor complex ligand to the dimer can be prepared on a multigram scale through a Diels-Alder reaction,[10] 2) the method allows a range of complexes, including **5** and **6** (Figure 1) to be prepared efficiently[11] and, 3) the wider range of

complexes offer some advantages in the reductions of certain ketones, for example acetophenone derivatives containing an *ortho*-methoxy group.[7]



Scheme 2. Synthetic approach to tethered complexes *via* a hexadiene.

Recently, we reported the synthesis and catalytic applications of tethered complex **7** containing a benzyl-tethered structure, however the synthesis required the lengthy formation of a 1,3-cyclohexadiene derivative (**8**) which was then complexed with $RuCl_3$ (Scheme 3).[12] The synthesis of **8** itself required three steps from 2-bromobenzaldehyde and cyclohexenone.

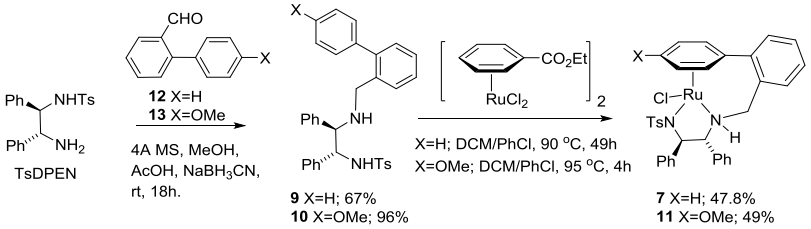


Scheme 3. Published synthetic approach to benzyl-tethered complexes, *via* a hexadiene.

In this paper, we report extensions of the arene-exchange methodology to a range of new complexes, notably those linked through a benzyl-tether as in complex **7**, which now allows these complexes to be accessed through a short route of just three linear steps from commercially-available starting materials. Further examples of the arene-exchange approach to new catalysts and examples of their extended applications in ATH reactions are also described.

Results and Discussion.

The ligand precursors (*R*,*R*)-**9** and (*R*,*R*)-**10** to the known complex (*R*,*R*)-**7** and the novel *p*-methoxy derivative (*R*,*R*)-**11** respectively were made by reductive amination of TsDPEN with *o*-phenylbenzaldehyde **12** and *o*-(*p*-methoxyphenyl)benzaldehyde **13**; the latter prepared by a Pd-catalysed Suzuki coupling of *o*-bromobenzaldehyde with *p*-methoxyphenylboronic acid.[13] Using the arene-substitution method with the ruthenium dimer $[(C_6H_5CO_2Et)RuCl_2]_2$,[7,10] we were able to form the known complex (*R*,*R*)-**7** in just two linear steps from TsDPEN (Scheme 4). The novel *p*-methoxyphenyl tethered complex (*R*,*R*)-**11** was prepared on a >700 mg scale and its structure was confirmed by X-ray crystallographic analysis (Figure 2). In common with the majority of complexes of this type, the configuration at the Ru atom (*S*) is controlled by the stereochemistry of the diamine ligand, with the Ru-Cl and N-H bonds being on the same side and approximately parallel to each other. Complex (*R*,*R*)-**11** appears to be formed as a single diastereoisomer. In reductions with Ru (II)/TsDPEN complexes of this type, under catalytic conditions the hydride is generated.[14] Through this process, the chirality is efficiently transferred to the product in the subsequent hydrogen-transfer process (*vide infra*).



Scheme 4. Synthesis of benzyl-tethered catalysts (*R*,*R*)-**7** and (*R*,*R*)-**11** *via* an arene-exchange route.

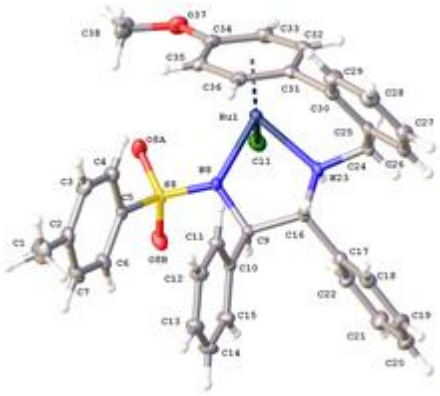
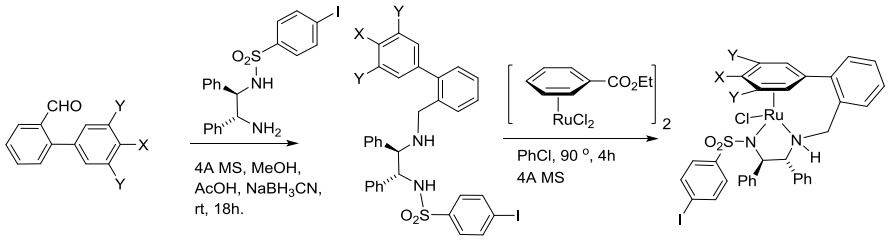


Figure 2. X-ray crystallographic structure of benzyl-tethered catalyst (*R*,*R*)-**11**.

We also prepared complexes (*R*,*R*)-**14,** (*S*,*S*)-**15** and (*S*,*S*)-**16**, containing the benzyl tether but with a *p*-iodophenylsulfonyl group (IPS) in place of *p*-toluenesulfonyl (Ts) (Scheme 5). These complexes have the potential to be attached to supports such as soluble polymers through Pd-catalysed coupling reactions,[13] and proved to be equally stable and facile to isolate whilst exhibiting excellent reactivity and enantioselectivity. Their synthesis followed essentially the same route as before, from the IPS ligands **17**-**19** respectively which were in turn prepared using aldehydes **13**, **20** and **21**.[15-17] Again, the new aldehydes were prepared through a Pd-catalysed Suzuki coupling reaction of 2-bromobenzaldehyde with the corresponding methoxy-substituted boronic acids.[13]



Scheme 5. Synthesis of IPS catalysts (*R*,*R*)-**14**, (*S*,*S*)-**15** and (*S*,*S*)-**16** *via* an arene-exchange route. Although the synthesis illustrates the (*R*,*R)*-enantiomer, (*S*,*S*)-**15** and **16** were prepared in this study.

In addition, we have examined the extension of the scope of the arene-substitution process to catalysts (*R*,*R*)-**22**-**24** containing the more established three-carbon saturated hydrocarbon tether *via* the reaction of the respective ligands (*R*,*R*)-**25**-**27** with $[(C_6H_5CO_2Et)RuCl_2]_2$[10] (Figure 3). The use of the iodo-substituted sulfonamide was also tolerated in this reaction and in addition a derivative containing a TMS-protected acetylene group ((*R*,*R*)-**23**) was prepared. To assist the aqueous solubility of the catalyst, which may be valuable in certain applications, complex (*R*,*R*)-**24** containing a PEG chain was also prepared (Figure 3) using the arene-exchange methodology.

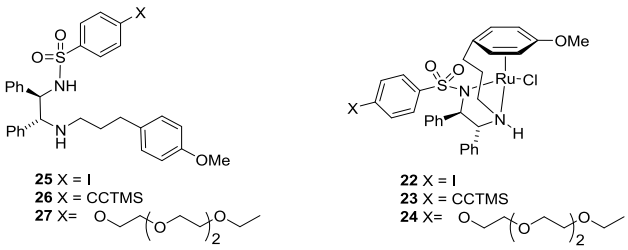


Figure 3. Iodo, alkyne and PEG-containing tethered Ru (II) complexes containing the aliphatic 3-carbon tether, and their respective ligand precursors.

Given the promising results obtained using TsDPEN and its close derivatives, we examined the application of the arene-exchange method to the synthesis of racemic complexes. In attempts to prepare precursor ligands, the reaction of $TsNHCH_2CH_2NH_2$ (TsEN) with 3-(4-methoxyphenyl)propanol proved frustrating due to multiple alkylation reactions, whether either the triflate intermediate strategy or the reductive amination approach were employed. It was however possible to complete the formation of the benzyl-tethered ligands in high yield and subsequently complexes **28**-**30** (Figure 4). Racemic complexes containing a linear three-carbon tethers have been reported previously,[1d,1e] however the arene-exchange application was extended to the synthesis of three new complexes **28** – **30**, two of which contain the larger tri-isopropyl-phenyl sulfonyl (Tris) group (Figure 4). The X-ray crystallographic structure of the benzyl-tethered complex **29** was also obtained (Figure 5).

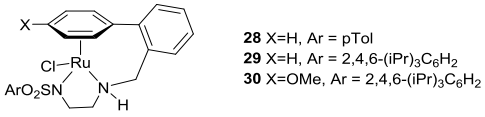


Figure 4. Racemic catalysts formed *via* the arene-exchange approach.

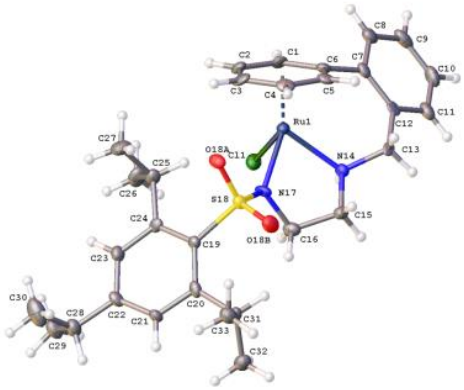
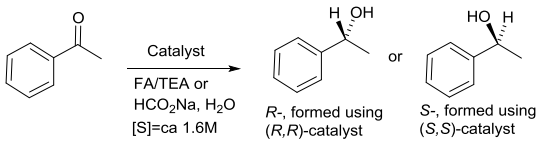


Figure 5. X-ray of racemic, benzyl-tethered triisopropylphenylsulfonyl complex **29**.

All of the catalysts were tested against acetophenone to establish that they were efficient in this capacity, using the 5:2 formic acid/triethylamine azeotrope (FA/TEA) as both solvent and reducing agent (Table 1). The applications of the unsubstituted benzyl-tethered complex **7** have already been reported.[12] The new *p*-OMe complex (*R,R*)-**11** gave equally good results, reducing acetophenone in up to 98% ee. Using the IPS derivative (*R,R*)-**14**, acetophenone was reduced with an enantioselectivity of 96.8% and a 99.7% conversion after 24 h. These results compare favorably in terms of enantioselectivity and conversion to those achieved by both the original '3C'-tethered catalyst **1**[1] and the *p*-methoxy-3C tethered catalyst **5**.[7] Slightly lower conversions and enantioselectivities were observed using the *m*-methoxy substituted catalysts (*S,S)*-**15** and (*S,S)*-**16**. This was not unexpected[1,7] and is discussed later in this paper. All three catalysts (*R,R*)-**22-24** gave reduction products in essentially complete conversion, and ees in excess of 96%.

Table 1. ATH of acetophenone using catalysts (*R,R*)-**11**, (*R,R*)-**14**, (*S,S*)-**16** and (*R,R*)-**22-24**.[a]



Entry	Catalyst	S/C	solvent	Temp / °C	Time /h	Conv / %	Ee / %
1	(*R,R*)-**11**	200	FA/TEA	40	24	100	98 (*R*)
2	(*R,R*)-**14**	100	FA/TEA	40	24	>99	97 (*R*)
3	(*S,S*)-**15**	100	FA/TEA	40	51	96	93 (*S*)
4	(*S,S*)-**16**	100	FA/TEA	40	51	90	89 (*S*)
5	(*R,R*)-**22**	100	FA/TEA	40	7	>99	97 (*R*)
6	(*R, R*)-**23**	100	FA/TEA	40	22	>99	96 (*R*)
7	(*R, R*)-**24**	100	FA/TEA	40	4	>99	97 (*R*)
8	(*R, R*)-**24**	100	H_2O	60	1	99	97 (*R*)
9	(*R, R*)-**24**	100	H_2O:MeOH (1:1)	60	1	95	97 (*R*)
				60	2	99	97 (*R*)
10	(*R, R*)-**24**	500	H_2O:MeOH (1:1)	60	3	33	97 (*R*)
				60	25.5	88	96 (*R*)

a. conversion and ee determined by GC. Entries 8-10; sodium formate (5 eq.) was used as the hydrogen source.

The PEG-containing catalyst (*R*,*R*)-**24** was also tested in aqueous solution (Table 1) and gave excellent results in this medium. Under these conditions, sodium formate was used in place of formic acid as the hydrogen source. In these reactions either water or a water/methanol mixture could be used as solvent and 99% conversion to a product of 97% ee could be achieved within 2h. At a lower loading of 0.2 mol%, 88% conversion/96% ee was achieved after 25.5h.

The new complexes (*R*,*R*)-**11,** (*R*,*R*)-**14** were tested in a wider range of ATH reactions focussing predominantly on acetophenone derivatives (Figure 6). In these reductions (Table 2) typically 1 mol % of catalyst was used at 45°C in the 5:2 formic acid/triethylamine azeotrope (FA/TEA) however in the case of (*R,R)*-**11**, a lower catalyst loading was also used in order to test the practicality of the method; at this level, 250-300 mg of substrate requires just ca. 3 mg of catalyst. Although not all substrates were tested with all catalysts at lower loadings, we are confident that they exhibit similar activity. The dimethoxy and trimethoxy catalysts (*S*,*S*)-**15** and (*S*,*S*)-**16** were also used in the reductions of representative ketones (Table 2).

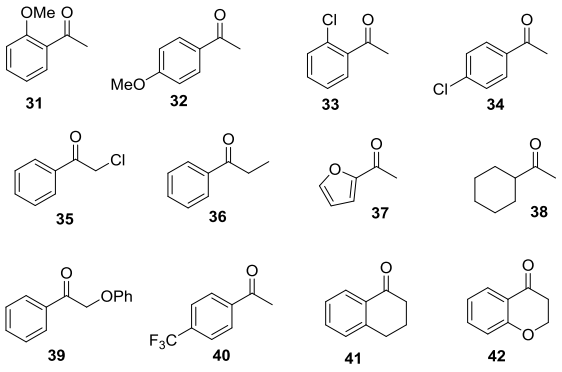
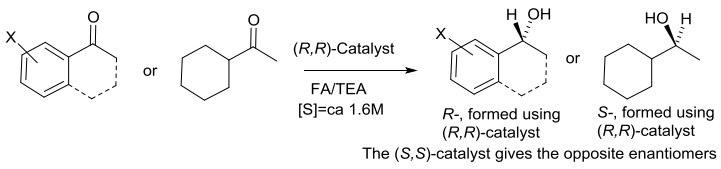


Figure 6. Ketones reduced using complexes (*R*,*R*)-**11**, (*R*,*R*)-**14**, (*S*,*S*)-**15** and (*S*,*S*)-**16**.

Table 2. Ketone reductions using (*R*,*R*)-**11**, (*R*,*R*)-**14**, (*S*,*S*)-**15** and (*S*,*S*)-**16**.



Entry	Ketone	Catalyst	S/C	Time /h	Conv /%[a]	Yield /%	ee /%[a]
1	Acetophenone	(*R*,*R*)-**11**	400	72	100	84	98 (*R*)
2	*o*-OMe **31**	(*R*,*R*)-**11**	400	72	100	73	87 (*R*)
3	*p*-OMe **32**	(*R*,*R*)-**11**	400	72	100	82	99 (*R*)
4	*o*-Cl **33**	(*R*,*R*)-**11**	400	72	100	87	90 (*R*)
5	*p*-Cl **34**	(*R*,*R*)-**11**	400	72	100	67	87 (*R*)
6	α-Cl **35**	(*R*,*R*)-**11**	400	72	100	79	97 (*S*)
7	PhCOEt **36**	(*R*,*R*)-**11**	400	72	100	86	94 (*R*)
8	Furyl **37**	(*R*,*R*)-**11**	400	72	100	59	99 (*R*)
9	Cyclohex **38**	(*R*,*R*)-**11**	400	72	100	88	48 [c] (*S*)
10	OPh **39**	(*R*,*R*)-**11**	400	72	100	75	93 (*S*)
11	*p*-CF_3 **40**	(*R*,*R*)-**11**	400	72	100	79	95 (*R*)
12	Tetralone **41**	(*R*,*R*)-**11**	400	72	100	86	99 (*R*)
13	Chromanone **42**	(*R*,*R*)-**11**	400	72	100	78	99 (*R*)
14	Acetophenone	(*R*,*R*)-**14**	100	23	>99	68	97 (*R*)
15	*o*-OMe **31**	(*R*,*R*)-**14**	100	23	97	65	87 (*R*)
16	*p*-OMe **32**	(*R*,*R*)-**14**	100	23	94	72	96 (*R*)
17	*o*-Cl **33**	(*R*,*R*)-**14**	100	25	>99	61	88 (*R*)
18	*p*-Cl **34**	(*R*,*R*)-**14**	100	21.5	99	63	94 (*R*)
19	α-Cl **35**	(*R*,*R*)-**14**	100	26	>99	59	97 (*S*)
20	PhCOEt **36**	(*R*,*R*)-**14**	100	26	99	51	94 (*R*)
21	Furyl **37**	(*R*,*R*)-**14**	100	21.5	99	65	94 (*R*)
22	Cyclohex **38**	(*R*,*R*)-**14**	100	41	>99	60	46[c] (*S*)
23	*o*-OMe **31**	*(S,S)*-**15**	100	65	86	n/a[d]	68 (*S*)
24	*o*-OMe **31**	*(S,S)*-**16**	100	65	76	n/a[d]	87 (*S*)
25	*p*-OMe **32**	(*S*,*S*)-**15**	100	65	82	n/a[d]	82 (*S*)
26	*p*-OMe **32**	(*S*,*S*)-**16**	100	65	93	n/a[d]	85 (*S*)
27	Cyclohex **38**	(*S*,*S*)-**15**	100	41	97	60	71[c] (*R*)
28	Cyclohex **38**	(*S*,*S*)-**16**	100	41	44	n/a[d]	51[c] (*R*)

a) conversion and ee determined by GC. c) ee determined by acetylation of alcohol followed by GC. d. the reduction product was not isolated.

With the exception of acetyl cyclohexane (cyclohexyl methyl ketone; Table 1), the absolute sense of all of the reductions using *(R,R)*-**11** and *(R,R)*-**14** are likely to result from similar range of interactions in the reduction transition state (TS). Recent detailed computation work has revealed that a combination of stabilization of the favored TS by electrostatic catalyst/substrate CH/π interactions and a more significant destabilization of the disfavored TS by SO_2 lone pair/π repulsion (both illustrated in Figure 7).[14]

Because this stabilization is not available to cyclohexyl methyl ketone, this substrate represents a challenging substrate for ATH catalysts.[1] The reduction of acetyl cyclohexane proceeds with significantly reduced ee because the enantioselectivity between the two faces of the ketone is not determined by electrostatic effects involving an arene ring in the substrate. Although the control is weaker, the favored reduction TS is likely to be stabilized by SO_2 lone pair/C-H attraction, (Figure 8), resulting in formation of the (*S*)-enantiomer of the product using (*R,R*)-configuration catalysts. The reduction of α-chloro and α–phenoxyacetophenone, however, produces the (*S*)-enantiomer despite being stabilized by CH-π interactions (Figure 7), due to reversal of the Cahn-Ingold-Prelog priorities of the groups.

It was anticipated, given the precedents in this area, that the di- and trimethoxy catalysts (*S,S*)-**15** and (*S,S*)-**16** would exhibit reduced selectivity for the ATH of acetophenone derivatives, owing to a reduction in the stabilization of the favored TS by an increase in the steric hindrance around the η^6-arene ring (Figure 7). In the event a small decrease in ee was observed. The configurations are of course reversed relative to the other catalysts because of the change of the absolute configuration of the catalyst. However this modification would be predicted to increase the selectivity of cyclohexyl methyl ketone reduction due to the increase of steric hindrance in the same region (Figure 8) and indeed this proved to be the case (Table 2).[1f,7]

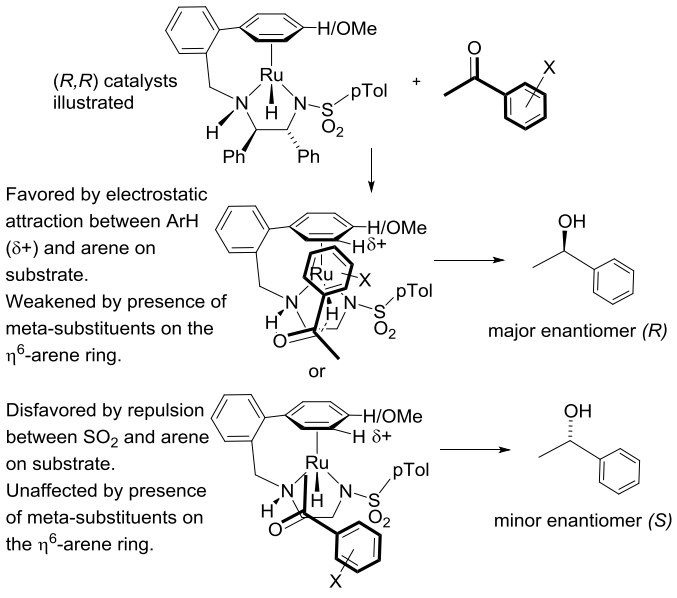


Figure 7. Interactions between asymmetric catalysts and acetophenone derivatives, with the favored mode of reduction illustrated.[14]

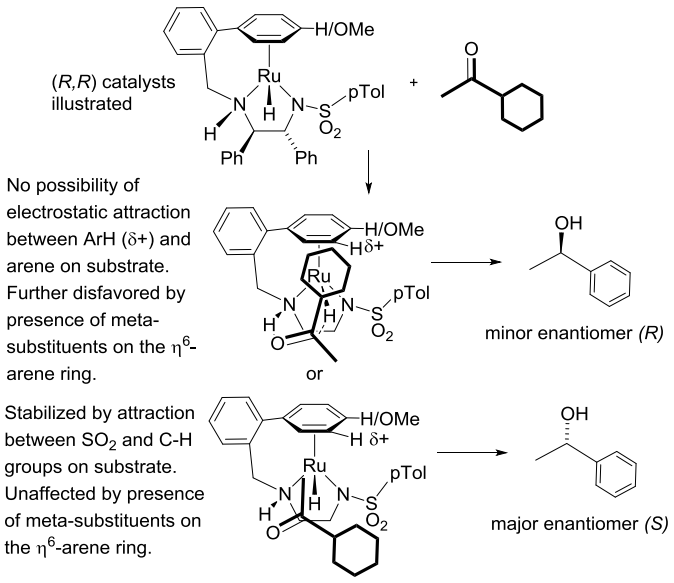


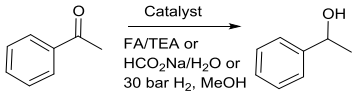
Figure 8. Interactions between asymmetric catalysts and acetyl cyclohexane, with the favored mode of reduction illustrated.[14]

Ortho-substituted acetophenone derivatives were reduced with the lowest enantioselectivities, with *o*-methoxyacetophenone **31**, and *o*-chloroacetophenone **33** being reduced in 87% and 90% respectively by (*R,R)*-**11** and 87% and 88% ee by (*R,R)*-**14**. This reduction of enantioselectivity is most likely due to the increased steric hindrance around the ketone. It is noteworthy, however, that reduction of *o*-methoxyacetophenone using the trimethoxy catalyst (*S,S*)-**16**, exhibits very similar enantioselectivity to the methoxy catalysts (*R,R*)-**11** and (*R,R)*-**14** (87% ee) whereas the dimethoxy catalyst (*S,S)*-**15** gave the product of lowest ee (66% ee). This indicates that a secondary effect from the *p*-methoxy group on the catalyst, with this particular substrate, might be operating.

The novel racemic catalysts **28-30** were tested in the reduction of ketones using both transfer hydrogenation and hydrogenation with hydrogen gas, and proved to be competent catalysts. Even at loadings as low as S/C = 500, near-complete reduction was achieved using FA/TEA although higher loadings were used to ensure full reduction. In the hydrogenation tests, again at S/C = 500 loadings, reductions were

complete within 16h, although the conversions dropped off significantly at the lower loading of S/C = 1000 (Table 3).

Table 3. Acetophenone reduction using racemic catalysts **28**-**30**.



Entry	Catalyst	Reagent	Solvent	S/C	Temp / °C	Time / h	Conv / %
1	**28**	FA:TEA	-	100	28	24.5	100
2	**29**	FA:TEA	-	100	28	6 h	35
3	**29**	FA:TEA	-	100	28	23 h	100
4	**29**	FA:TEA	-	500	60	4.5 h	99
5	**29**	FA:TEA	-	500	60	5.0 h	99
6	**30**	FA:TEA	-	500	60	4.0 h	100
7	**29**	HCOONa	H_2O	100	40	6 h	100
8	**29**	HCOONa	H_2O	100	60	1.5 h	>99
9	**30**	HCOONa	H_2O	100	60	2.5 h	100
10	**29**	H_2 gas	MeOH	250	60	16 h	>99
11	**29**	H_2 gas	MeOH	500	60	16 h	99
12	**29**	H_2 gas	MeOH	1000	60	16 h	21
13	**30**	H_2 gas	MeOH	250	60	16 h	>99
14	**30**	H_2 gas	MeOH	500	60	16 h	100
15	**30**	H_2 gas	MeOH	1000	60	16 h	77.3

In conclusion, we have demonstrated that a series of benzyl-tethered arene/Ru (II)/TsDPEN complexes, which are difficult to prepare through the hexadiene approach, may be readily prepared using the alternative arene-swapping method that we have recently developed. These complexes, and related racemic derivatives, are competent catalysts for the asymmetric transfer hydrogenation of ketones, and for the racemic reduction of ketones *via* transfer hydrogenation or hydrogenation with hydrogen gas at low loadings.

Experimental section.

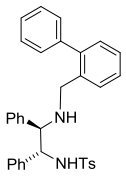
General Experimental.

All reagents and solvents were used as purchased and without further purification. All reactions were carried out under a nitrogen atmosphere unless otherwise specified. Reactions at elevated temperature were maintained by thermostatically controlled aluminium heating blocks. A temperature of 0 °C refers to an ice slush bath. NMR spectra were recorded on a Bruker AV (250 MHz), Bruker DPX (300 or 400MHz), Bruker DRX (500 MHz) or Bruker AV-II. (700 MHz). All chemical shifts are reported in ppm and are referenced to the solvent chemical shift, and coupling constants are given in Hz. Mass spectra were recorded on an Esquire 2000 and high resolution mass spectra were recorded on a Bruker Micro ToF or MaXis. IR spectra were recorded on a PerkinElmer spectrum100 and peaks are reported in wavenumbers. The optical rotations were measured on an Optical Activity Ltd. AA-1000. The chiral GC measurements were done on a PerkinElmer 8500 or Hewlett-Packard 1050 instrument linked to PC running DataApex Clarity software. Melting points were determined on a Stuart scientific melting point apparatus and are uncorrected. Flash column chromatography was performed using silica gel of mesh size 230-400, Thin layer chromatography was carried out on aluminium backed silica gel 60 (F254) plates, visualized using 254nm UV light or iodine stains as appropriate.

Dichloro(ethylbenzoate) ruthenium (II) dimer.[10]

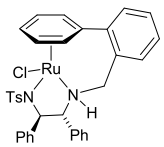
Ethyl 1,4-cyclohexadene-1-carboxylate (1.04 g, 6.19 mmol, 4.1eq.) and ruthenium trichloride hydrate (0.398 g, 1.52 mmol assuming x=3, 1 eq.) were combined together in a dried and nitrogen purged flask connected to a condenser. Dry EtOH (20 mL) was then added, and the reaction was stirred at reflux for 22 h. The reaction was cooled and filtered and the solid residue was washed with hexane and Et_2O to leave the product as an orange solid (0.433g, 0.67 mmol, 88.3%). Mp 233.1-237.4°C; ν_{max}: 3078, 2999, 2988, 2945, 2900, 1720, 1512, 1469, 1396, 1287, 1267, 1104, 1021, 977 cm^{-1}; δ_H (400 MHz, DMSO-d6) δ ppm 6.69 (2 H, d, *J* 6.1, *o*-Ar*H*), 6.29 (1 H, t, *J* 5.7, *p*-Ar*H*), 6.04 (2 H, t, *J* 6.1, *m*-Ar*H*), 4.34 (2 H, q, *J* 7.1, CH_2), 1.32 (4 H, t, *J* 7.1, CH_3); δ_C (126 MHz, $CDCl_3$) δ ppm 164.35, 92.95, 92.30, 85.69, 82.96, 62.59, 40.49, 40.32, 40.15, 39.99, 39.82, 39.65, 39.48, 14.73.

((*R*,*R*)-2-*N*-(([1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-methylbenzene-sulfonamide **9**.



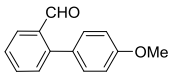
To a mixture of (*R*,*R*)-TsDPEN (0.200 g, 0.546 mmol, 1.0 eq) and MS 4Á (0.4 g) in dry methanol (10 mL) was added biphenyl-2-carboxaldehyde (0.101 mL, 0.628 mmol, 1.15 eq) followed by acetic acid (2-3 drops). The mixture was stirred at room temperature under an inert atmosphere for 4.5 h to form the imine. To this, $NaBH_3CN$ (0.142 g, 2.266 mmol, 4.15 eq) was added and resulting mixture was stirred at room temperature for 18 h. The reaction mixture was filtered and concentrated to give a residue. This was dissolved in DCM (20 mL) and washed with 1M NaOH (2 x 15 mL), dried over anhydrous Na_2SO_4, filtered and the solvent removed to give the crude product. The crude compound was purified by flash column chromatography over silica gel using EtOAc: Pet. ether (7:3) to give (*R*,*R*)-**9** as white solid (0.195 g, 0.367 mmol, 67%). HRMS: found 533.2262 ($C_{34}H_{32}N_2O_2S$ H+ requires 533.2257, error = -0.3 ppm); ν_{max} 3265, 3059, 3028, 2855, 1598, 1453, 1324, 1153, 1090, 916, 748, 666 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.33-7.27 (7H, m, -C*H* of phenyl), 7.21-7.17 (2H, m, -C*H* of phenyl), 7.12-7.09 (4H, m, -C*H* of phenyl), 7.05-7.01 (4H, m, -C*H* of phenyl), 6.96 (2H, d, *J* 8.4, -C*H* of phenyl), 6.88-6.86 (2H, m, -C*H* of phenyl), 6.75-6.73 (2H, m, -C*H* of phenyl), 5.88 (1H, br d, *J* 3.4, -N*H*Ts), 4.17 (1H, dd, *J* 6.6, 3.4, -C*H*NHTs), 3.52 (1H, d, *J* 12.6, -CHNHC*H*H-), 3.51 (1H, d, *J* 6.6, -C*H*NHCH_2-), 3.29 (1H, d, *J* 12.6, -CHNHCH*H*-), 2.31 (3H, s, -CH_3), 1.39 (1H, br s, -N*H*-CH_2-) ppm; δ_C (100 MHz, $CDCl_3$) 142.59, 142.22, 141.07, 138.79, 138.50, 137.06, 136.72 (all C to here), 130.11, 130.11, 129.67, 129.15, 129.07, 128.84, 128.44, 128.30, 128.28, 127.98, 127.75, 127.70, 127.49, 127.39, 126.98 (all ArCH), 67.21 (CH). 63.03 (CH), 48.98 (CH_2), 21.44 (CH_3) ppm. m/z ESI-MS $[M+H]^+$ 533.2.

N-((*R*,*R*)-2-(([1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-methylbenzene-sulfonamide ruthenium (II) chloride complex **7**.[12]



((*R*,*R*)-2-*N*-(([1,1'-Biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide **9** (0.050 g, 0.094 mmol, 1.0 eq) and [Ru ($C_6H_5CO_2Et$)Cl_2]$_2$ (0.030 g, 0.047 mmol, 0.5 eq) in dry DCM (1.5 mL) was placed in a glass tube under N_2. The tube was sealed and mixture was stirred at room temp for 30 min to give a brick red solution and heated at 90 ^oC for 49 h. The reaction was followed by TLC and mass spectrometric analysis. The reaction mixture was cooled to room temperature and concentrated to give dark brown residue. The residue was dissolved in diethyl ether, then the solvent volume was reduced in order to precipitate the crude product, which was isolated by filtration and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 85:15) to give (*R*,*R*)-**7** as a brown solid (0.030 g, 0.045 mmol, 47.8%). HRMS: found 633.1159 ($C_{34}H_{31}N_2O_2RuS$-Cl+ requires 633.1153, error = -1.4 ppm); δ_H (300 MHz, $CDCl_3$) 7.61-7.53 (2H, m, ArH), 7.42-7.37 (1H, m, ArH), 7.21 (2H, d, *J* 8.1, *m*-C*H*-SO_2-ArH), 7.16-7.10 (3H, m, ArH), 6.91 (1H, d, *J* 7.5, ArH), 6.79 (2H, d, *J* 8.1, *o*-C*H*-SO_2ArH), 6.75-6.70 (3H, m, 2-C*H*-ArH, -C*H* of Ru-Ar), 6.62-6.57 (3H, m, -ArH), 6.44 (2H, d, *J* 7.2, ArH), 6.11-6.02 (2H, m, -C*H* of Ru-Ar), 5.18 (1H, d, *J* 5.7, -C*H* of Ru-Ar), 5.10 (1H, d, *J* 5.0, -C*H* of Ru-Ar), 4.95 (1H, d, *J* 12.0, -CHN*H*-CH_2-), 4.70 (1H, *J* 13.5, -NH-C*H*H-), 4.10 (1H, d, *J* 11.3, -C*H*NTs), 3.85 (1H, d, *J* 13.5, -NH-CH*H*-), 3.25 (1H, dd, *J* 12.0, 11.3, -C*H*NH-CH_2-), 2.21 (3H, s, -CH_3) ppm; δ_C (75 MHz, $CDCl_3$): 141.18, 138.73, 137.94, 134.73, 133.12, 132.30, 131.08, 129.38, 129.15, 128.77, 128.14, 128.03, 127.30, 126.81, 126.22, 125.73, 96.06 (RuAr), 94.77 (RuAr), 94.63 (RuAr), 78.27 (RuAr), 77.15 (RuAr), 75.71 (CH), 68.45 (CH), 52.89 (CH_2), 20.61 (CH_3); m/z ESI-MS $[M\text{-}Cl]^+$ 633.1.

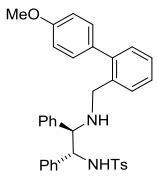
4'-Methoxy-diphenyl-2-carbaldehyde **13**.[15]



Methoxyboronic acid (0.246g, 1.62 mmol, 1.18 eq.), palladium tetrakis (0.022g, 0.019 mmol, 0.014 eq.) and sodium carbonate (0.214g, 2.02 mmol, 1.46 eq.) were dissolved in DMF (10 mL). 2-Bromobenzaldehyde (0.255 g, 1.38 mmol, 1 eq.) was added dropwise over 5 minutes into the mixture, which was then stirred at 156 °C for 20 h. The mixture was allowed to cool to room temperature before ethyl acetate (50 mL) then a saturated solution of sodium bicarbonate (30 mL) was added. Following extraction

with ethyl acetate (2 × 30 mL), the organic extracts were washed with brine (4 × 25 mL), dried (anhydrous sodium sulfate) and concentrated under reduced pressure to give an oil. The crude product was purified by column chromatography on silica, (8.03g silica, eluation using 200 mL 10% EtOAc/Pet ether) to give as a white powder, 4'-methoxy-diphenyl-2-carbaldehyde **13** (0.25g, 1.18 mmoles, 86%). TLC: 20% EtOAc/Petroleum Ether, silica, Rf =0.36, UV light; Mp 52.8-53.7°C; ν_{max}: 2999, 2974, 2938, 2752, 1683, 1595, 1509, 1441, 1393, 1296, 1242, 1183, 1030 cm^{-1}; δ_H (300 MHz, $CDCl_3$) δ 10.01 (1 H, s, *H*COAr), 8.02 (1 H, d, *J* 7.7, ArH), 7.59 - 7.68 (1 H, t, *J* 7.4, ArH), 7.42 - 7.52 (2 H, m, ArH), 7.32 (2 H, d, *J* 7.5, *o*-*H*-Ar -OMe), 7.02 (2 H, d, *J* 7.5, *m*-*H*-Ar-OMe), 3.89 (3 H, s, CH_3) ppm; δ_C (126 MHz, $CDCl_3$) δ 192.68, 159.71, 145.67, 133.77, 133.54, 131.31, 130.80, 130.03, 127.63, 127.39, 113.95, 77.47, 77.04,76.62, 55.41 ppm; *m/z* (ESI+): 235.0 ($(M+Na)^+$, 100%).

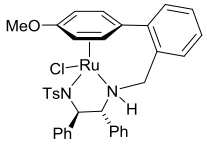
<u>((*R*,*R*)-2-*N*-((4'-methoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide **10**.</u>



To a solution of 4'-methoxy-diphenyl-2-carbaldehyde **13** (2.02 g, 9.50 mmol) and (*R*,*R*)-TsDPEN (3.48 g, 9.52 mmol) in MeOH (25 mL) at rt, a few drops of CH_3CO_2H were added. The mixture was stirred overnight then $NaBH_4$ (800 mg, 20.00 mmol) was added, along with MeOH (20 mL). The reaction was stirred at room temperature for 18 h, after which the MeOH was removed by evaporation. The reaction was quenched with sat. aq. $NaHCO_3$ (150 mL) and extracted with EtOAc (3 × 150 mL). The combined organic layers were washed with sat NaCl (100 mL), dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel column chromatography (eluent hexane/EtOAc=4:1-3:1) to afford (*R*,*R*)-**10** as white solid (5.10 g, 9.07 mmol, 96%). $[\alpha]_D^{24}$ -27.6 (c 0.4 in $CHCl_3$) (*R*); MP 57 °C; (found (ESI): M^+ + H, 563.2363. $C_{35}H_{34}N_2O_3S$ requires M, 563.2363); ν_{max} 3258, 3027, 1242, 1153, 762, 698, 666, 559, 546 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.31-6.99 (14H, m, ArH), 6.95 (2H, d, *J* 8.0, ArH), 6.89-6.82 (4H, m, ArH), 6.78-6.75 (2H, m, ArH), 5.97 (1H, br, NHTs), 4.18 (1H, d, *J* 7.5, C*H*NHTs), 3.83 (3H, s, OCH_3), 3.54 (1H, d, *J* 12.2, *H*CH), 3.53 (1H, d, *J* 7.2, C*H*NH), 3.29 (1H, d, *J* 12.2, *H*CH), 2.93 (3H, s, CH_3), 1.44 (1H, br, NH); δ_C (100 MHz,

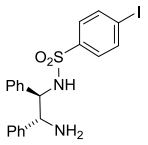
$CDCl_3$) 158.7, 142.6, 141.9, 138.8, 138.5, 137.0, 136.9, 130.4, 129.9 (2C), 129.8, 129.1 (2C), 128.3 (2C), 128.0 (2C), 127.5 (2C), 127.4 (4C), 127.3 (2C), 127.0 (2C), 113.7 (2C), 67.3, 63.1, 55.3, 49.1, 21.5; *m/z* (ESI-MS) 563.1 $(M+H)^+$.

N-((*R*,*R*)-2- ((4'-methoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide ruthenium (II) chloride complex **11**.



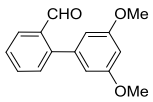
$[Ru(C_6H_5CO_2Et)Cl_2]_2$ (674 mg, 1.06 mmol) and (*R,R)*- 2- ((4'-methoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-methylbenzenesulfonamide **10** (1.79 g, 3.07 mmol) were dissolved in CH_2Cl_2 (80 mL), after 0.5 h, CH_2Cl_2 was removed and chlorobenzene (180 mL) was added. The degassed mixture was heated to 95 °C for 4h then the solvent was removed by evaporation. The resulting solid was purified by silica gel column chromatography (eluent first CH_2Cl_2/EtOAc=6:1 to remove excess ligand and then CH_2Cl_2/MeOH=30:1) to afford (*R,R)*-**11** as a brown powder (734 mg, 1.02 mmol, 49%). HRMS: (found (ESI): $(M-Cl^-)^+$, 663.1259. $C_{35}H_{33}N_2O_3RuS$ requires M, 663.1255); ν_{max} 3196, 1543, 1276, 1249, 1130, 1028, 698, 665, 577 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.65 (1H, d, *J* 7.5, ArH), 7.57 (1H, t, *J* 7.5, ArH), 7.42 (1H, t, *J* 7.5, ArH), 7.22 (2H, d, *J* 8.1, ArH), 7.15-7.05 (3H, m, ArH), 7.00 (1H, d, *J* 7.5, ArH), 6.85 (2H, d, *J* 8.0, ArH), (1H, d, *J* , ArH), 6.72 (1H, t, *J* 7.2, ArH), 6.65 (1H, m, ArH), 6.58 (2H, t, *J* 7.9, ArH), 6.42 (1H, d, *J* 5.8, ArH), 6.39 (2H, d, *J* 7.7, Ru-ArH), 5.88 (1H, d, *J* 6.5, Ru-ArH), 5.42 (1H, d, *J* 5.8, Ru-ArH), 5.15 (1H, d, *J* 6.5, Ru-ArH), 4.90 (1H, d, *J* 12.2, NH), 4.62 (1H, dd, *J* 14.4, 2.2, CHNTsRu), 4.20 (3H, s, OCH_3), 4.10 (1H, d, *J* 11.4, *H*CH), 3.82 (1H, d, *J* 14.1, C*H*NH), 3.09 (1H, t, *J* 11.4, HC*H*), 2.93 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 142.2, 139.3, 138.5, 134.3, 132.6, 132.0 (2C), 130.3, 129.7, 129.5, 129.1 (2C), 128.7 (2C), 128.5, 128.0 (2C), 127.4 (2C), 126.6 (2C), 126.3 (2C), 81.3 (2C), 80.7 (2C), 76.6, 75.4, 69.1, 57.4, 53.9, 21.2; *m/z* (ESI-MS) $(M-Cl^-)^+$ 663.1.

((*S,S*)-*N*-2-Amino-1,2-diphenylethyl)-4-iodobenzenesulfonamide.



(*S,S)*-Diphenylethyldiamine (DPEN) (2.12 g, 10 mmol, 1 eq) was added to potassium carbonate (1.38 g, 10 mmol, 1 eq) in DCM (30 mL) and water (25 mL) and this was then degassed. 4-Iodo-benzenesulfonyl chloride (3.05g, 10 mmol) in DCM (20 mL) was added dropwise, while stirring at 0°C, over 25 min. The mixture was allowed to warm to room temperature and stirred for 4 days, and monitored by TLC. Before neutralisation by saturated aqueous ammonium chloride (25 mL) and stirring for 3 days. Following extraction with DCM (4 × 100 mL), dried (Na_2SO_4) and filtered then concentrated under reduced pressure to give the product as white crystals. (4.73 g, 9.88 moles, 99.01 %). TLC: 50% EtOAc/Petroleum Ether, silica, Rf =0.1, UV light; Mp 180.8 – 182.4°C; $[\alpha]^D$ 6.18 (*c* 0.06 in $CHCl_3$) (*R,R)*-enantiomer; HRMS: found (ESI): $[M + H]^+$, 479.0291. ($C_{20}H_{20}IN_2O_2S$ requires 479.0285); ν_{max}: 3335, 3021, 2873, 2853, 1570, 1451, 1318, 1148, 1091, 1053, 1022 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ 7.50 (2 H, d, *J* 8.6, I-ArH), 7.12 - 7.31 (11 H, m, ArH), 7.10 (2 H, d, *J* 8.7, SO_2-ArH), 6.15 (1 H, br. s., NH), 4.42 (1 H, d, *J* 4.5, CH), 4.19 (1 H, d, *J* 4.6, CH), 1.41 (2 H, br. s., NH_2) ppm; δ_C (126 MHz, $CDCl_3$) δ 141.18, 139.78, 139.19, 137.68, 128.57, 128.47, 128.11, 127.60, 126.84, 126.30, 99.25, 77.27, 77.01, 76.76, 63.05, 60.22 ppm; *m/z* (ESI+): 479 ($(M+H)^+$, 100%).

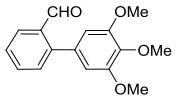
3',5'-Dimethoxy-diphenyl-2-carbaldehyde **20**.[16]



3,5-Dimethoxyboronic acid (0.232g, 1.27 mmol, 1.11 eq.), palladium tetrakis (0.011g, 0.010 mmol, 0.095 eq.) and sodium carbonate (0.174g, 1.64 mmol, 1.42 eq.) were combined in DMF (8 mL). 2-Bromobenzaldehyde (0.213 g, 1.15 mmol, 1 eq.) was added dropwise over 5 minutes into the mixture, which was then stirred at 155 °C for 21 h. The mixture was allowed to cool to room temperature before ethyl acetate (30 mL) then a saturated solution of sodium bicarbonate (20 mL) was added. Following extraction with ethyl acetate (4 × 30 mL), the organic extracts were washed with brine

(4 × 25 mL), dried (anhydrous sodium sulfate) and concentrated under reduced pressure to give an oil. The crude product was purified by column chromatography on silica, (16.5g silica, elution using 300 mL 10% EtOAc/Pet ether) to give 3',5'-dimethoxy-diphenyl-2-carbaldehyde **20** (0.234g, 0.96 mmol, 84%) as a white powder. TLC: 12% EtOAc/Petroleum Ether, silica, Rf =0.39, UV light; Mp 74.5-75.9°C; ν_{max}: 3057, 3006, 2952, 2932, 2872, 2831, 2754, 1689, 1589, 1454, 1417, 1387, 1347, 1203, 1152, 1061, 1027 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm 10.02 (1 H, s, *H*COAr), 8.02 (1 H, dd, *J* 7.8, 0.9, ArH), 7.63 (1 H, dt, *J* 15.1, 7.6, ArH), 7.44 - 7.53 (2 H, m, ArH), 6.55 (1 H, t, *J* 2.3, *o,o-H*-Ar$(OMe)_2$), 6.52 (2 H, d, *J* 2.1, *o,p-H*-Ar$(OMe)_2$), 3.84 (6 H, s, $(CH_3)_2$); δ_C (126 MHz, $CDCl_3$) δ ppm 192.40, 160.62, 145.91, 139.77, 133.76, 133.47, 130.39, 127.87, 127.33, 108.43, 105.50, 100.02, 99.45, 77.26, 76.74, 55.46; *m/z* (ESI+): 265.1 ($(M+Na)^+$, 100%).

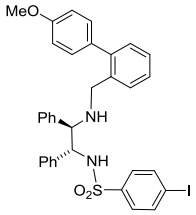
3',4',5'-Trimethoxy-diphenyl-2-carbaldehyde **21**.[17]



3,4,5-Trimethoxyboronic acid (0.754g, 3.56 mmol, 1.20 eq.), palladium tetrakis (0.036 g, 0.031 mmol, 0.011 eq.) and sodium carbonate (0.477g, 4.50 mmol, 1.52 eq.) were combined in DMF (20 mL). 2-Bromobenzaldehyde (0.549 g, 2.96 mmol, 1 eq.) was added dropwise over 5 minutes into the mixture which was then stirred at 170 °C for 18.5 h. The mixture was allowed to cool to room temperature before ethyl acetate (50 mL) then a saturated solution of sodium bicarbonate (30 mL) was added. Following extraction with ethyl acetate (6 × 30 mL), the organic extracts were washed with brine (4 × 50 mL), dried (anhydrous sodium sulfate) and concentrated under reduced pressure to give an oil. The crude product was purified by column chromatography on silica, (21.2g silica, eluation using 300 mL 12% EtOAc/Pet ether) to give 3',4',5'-trimethoxy-diphenyl-2-carbaldehyde **21** as a white powder (0.655g, 2.40 mmoles, 81%). TLC: 12% EtOAc/Petroleum Ether, silica, Rf =0.12, UV light; Mp 89.8-92.1°C; ν_{max}: 3059, 3003, 2969, 2940, 2839, 1681, 1582, 1507, 1454, 1410, 1346, 1292, 1237, 1122, 996 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ 10.02 (1 H, s, *H*COAr), 8.01 (1 H, dd, *J* 7.8, 0.9, ArH), 7.64 (1 H, td, *J* 7.6, 1.4, ArH), 7.45 - 7.52 (2 H, m, ArH), 6.57 (2 H, s, *o,p,o-H*-Ar- $(OMe)_3$), 3.92 (3H, s, *o,o*- $(OMe)_2$-Ar-O*C*H_3), 3.89 (6 H, s, (*o,m*- $(OMe)_2$-Ar-O*C*$H_3)_2$) ppm; δ_C (126 MHz, $CDCl_3$) δ 192.49, 153.12, 145.96, 138.01, 133.89, 133.51, 133.41, 130.51,

127.83, 127.47, 107.42, 77.29, 77.03, 76.78, 61.00, 56.26 ppm; *m/z* (ESI+): 295.0 ($(M+Na)^+$, 100%).

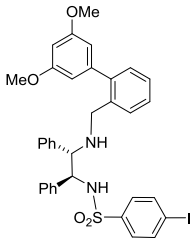
((*R,R*)-2-*N*-((4'-Methoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide **17**.



4'-Methoxy-diphenyl-2-carbaldehyde **13** (0.877g, 1.83 mmol, 1 eq.), (*R,R)-N*-(2-amino-1,2-diphenylethyl)-4-iodobenzenesulfonamide (0.406g, 1.91 mmol, 1.04 eq.) and 4Å-MS (1.127g) were combined in dry methanol (45 mL). Acetic acid (0.121 g, 2.01 mmol, 1.10eq.) was injected and the reaction mixture was stirred at room temperature for 6 h, and monitored by TLC. Then sodium cyanoborohydride (0.478g, 7.61 mmol, 4.15 eq.) was added in one portion and the reaction mixture was stirred for 4 days. The mixture was filtered through celite, concentrated and suspended in NaOH (1M, 88 mL) and extracted with DCM (6 × 90 mL). The combined organic extracts were washed with brine, dried (anhydrous sodium sulfate) and concentrated under reduced pressure to give the product (*R,R*)-**17** as a white solid (1.07g, 1.59 mmoles, 86.8 %). TLC: 20% ethyl acetate: 79% petroleum ether: 1% trimethylamine, silica, Rf =0.24, UV light; Mp 62.5-71.8 °C; $[\alpha]^D$ *(R)* -6.81 (c 0.43 in $CHCl_3$); HRMS: found (ESI): $[M + H]^+$ 675.1178. ($C_{34}H_{32}IN_2O_3S$ requires 675.1173); ν_{max}: 3273, 3060, 3027, 2934, 2834, 1610, 1569, 1514, 1453, 1242, 1157, 1088, 1034, 1004, 833, 762, 729, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm: 7.51 (2 H, d, *J* 8.5, *o*-I-ArH), 7.23 - 7.41 (3 H, m, ArH), 7.06 - 7.23 (10 H, m, ArH and *o*-SO_2-ArH), 7.04 (2 H, d, *J* 8.7, *o-H*-Ar -OMe), 6.92 (2 H, d, *J* 7.2, ArH), 6.87 (2 H, d, *J* 8.5, *m-H*-Ar-OMe), 6.80 (2 H, d, *J* 7.2, ArH), 6.01 (1 H, br. s. SO_2NH), 4.23 (1 H, d, *J* 6.7, CH), 3.88 (3 H, s, OC*H*$_3$), 3.53 - 3.59 (2 H, m, N-CH*H*-Ar and CH) 3.32 (1 H, d, *J* 12.2, N-CH*H*-Ar) 1.40 (1 H, br. s., NH); δ_C (126 MHz, $CDCl_3$): 158.93, 158.65, 141.87, 141.04, 139.83, 138.63, 138.16, 137.60, 137.37, 136.76, 133.55, 133.38, 133.00, 131.32, 130.80, 130.47, 130.24, 130.04, 129.84, 129.71, 128.57, 128.50, 128.40, 128.32, 128.15, 127.72, 127.64, 127.53, 127.47, 127.39, 127.33, 127.28, 126.98, 114.18, 113.95, 113.72, 99.29, 77.30, 77.04,

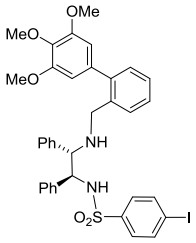
76.79, 67.13, 66.99, 63.34, 63.18, 63.10, 55.42, 55.32, 49.13, 48.82; m/z (ESI-): 673.0 ($[M - H^+]^-$, 100%), 709.0 ($(M+Cl^-)^-$, 30%).

N-((*S*,*S*)-2- ((3',5'-Dimethoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide **18**.



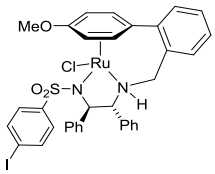
3',5'-Dimethoxy-diphenyl-2-carbaldehyde **20** (0.346g, 0.73 mmol, 1 eq.), (*S*,*S*)-*N*-((*S*,*S*)-2-amino-1,2-diphenylethyl)-4-iodobenzenesulfonamide (0.196g, 0.81mmol, 1.16 eq.) and 4Å-MS (0.442g) were added together in dry methanol (22 mL). Acetic acid (0.068 g, 1.13 mmol, 1.60 eq.) was injected and the reaction mixture was stirred at room temperature for 6 h, and monitored by TLC. Then sodium cyanoborohydride (0.186g, 3 mmol, 4.09 eq.) was added in one portion and the reaction mixture was stirred for 3 days. The mixture was filtered through celite, concentrated and suspended in NaOH (1M, 40 mL) and extracted with DCM (5 × 40 mL). The combined organic extracts were washed with brine, dried (anhydrous sodium sulfate) and concentrated under reduced pressure to give the product (*S*,*S*)-**18** a pink crystals (0.489g, 0.69 mmoles, 96.1 %). TLC: 20% ethyl acetate: 79% petroleum ether: 1% trimethylamine; Mp 71.7-74.6 °C; $[\alpha]^D$ *(S)* 6.64 (c 0.20 in $CHCl_3$); HRMS: found (ESI): $[M + H]^+$ 705.1289. ($C_{35}H_{34}IN_2O_4S$ requires 705.1279); ν_{max}: 3258, 3061, 3027, 3002, 2934, 2836, 1590, 1453, 1418, 1333, 1203, 1151, 1055, 1026, 1006, 927, 815, 763, 729, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm: 7.50 (2 H, d, *J* 8.5, *o*-I-ArH), 7.30 - 7.33 (2 H, m, ArH), 7.22 - 7.25 (1 H, m, ArH), 7.18 - 7.21 (1 H, m, ArH), 7.01 - 7.16 (8 H, m, ArH and *o*-SO_2-ArH), 6.86 (2 H, d, *J* 7.2, ArH), 6.76 (2 H, d,*J* 7.2, ArH), 6.47 (1 H, t, *J* 2.3, *o*,*o*-*H*-Ar- $(OMe)_2$), 6.36 (2 H, d, *J* 2.3, *o*,*p*-*H*-Ar- $(OMe)_2$), 6.04 (1 H, br. s., SO_2NH), 4.23 (1 H, d, *J* 7.3, CH), 3.78 (6 H, s, $(OCH_3)_2$), 3.56 - 3.65 (2 H, m, N-CH*H*-Ar and CH), 3.38 (1 H, d, *J* 12.7, N-CH*H*-Ar), 1.56 (1 H, br. s., CH-N*H*-CH_2); δ_C (126 MHz, $CDCl_3$): 160.50, 143.05, 141.87, 139.89, 138.60, 137.97, 137.52, 136.61, 130.02, 129.53, 128.33, 128.30, 128.02, 127.63, 127.47, 127.39, 127.35, 127.27, 127.19, 106.94, 99.30, 99.25, 77.25, 76.74, 67.16, 63.07, 55.36, 49.15; m/z (ESI+): 705.1 ($[M + H]^+$, 100%), 727.1 ($[M+Na]^+$, 10%).

N- ((*S*,*S*)-2- ((3',4',5'-Trimethoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide **19**.



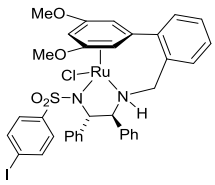
3',4',5'-Trimethoxy-diphenyl-2-carbaldehyde **21** (0.763g, 1.59 mmol, 1 eq.), ((*S*,*S*)-*N*-2-amino-1,2-diphenylethyl)-4-iodobenzenesulfonamide (0.507g, 1.86 mmol, 1.17 eq.), and 4Å-MS (0.943g) were added together in dry methanol (40 mL). Acetic acid (0.108 g, 1.8 mmol, 1.13 eq.) was injected and the reaction mixture was stirred at room temperature for 6.5 h, and monitored by TLC. Then sodium cyanoborohydride (0.432g, 6.873 mmol, 4.31 eq.) was added in one portion and the reaction mixture was stirred for 3 days. The mixture was filtered through celite, concentrated and suspended in NaOH (1M, 40 mL) and extracted with DCM (5 × 80 mL). The combined organic extracts were washed with brine, dried (anhydrous sodium sulfate) and concentrated under reduced pressure to give the product (*S*,*S*)-**19** as white crystals (0.890g, 1.21 mmoles, 76 %). TLC: 20% ethyl acetate: 79% petroleum ether: 1% trimethylamine; Mp 80.9-84.7 °C; $[\alpha]^{D}$ *(S)* -8.02 (c 0.29 in $CHCl_3$); HRMS: found (ESI): $[M + H]^+$ 735.1390 ($C_{36}H_{36}IN_2O_5S$ requires 735.1384); ν_{max}: 3269, 3238, 3059, 3027, 3000, 2932, 2834, 2332, 1570, 1453, 1407, 1342, 1236, 1156, 1123, 1005, 816, 765, 729, 698 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm: 7.48 (2 H, d, *J* 8.5, *o*-I-ArH), 7.31 - 7.35 (2 H, m, ArH), 7.24 (2 H, td, *J* 4.4, 1.3, ArH), 7.04 - 7.16 (6 H, m, ArH and *o*-SO_2-ArH), 7.06 (2 H, d, *J* 8.5, ArH), 7.02 (2 H, t, *J* 7.6, ArH), 6.85 (2 H, d, *J* 7.2, ArH), 6.73 (2 H, d, *J* 7.2, ArH), 6.40 (2 H, s, *H*-Ar- $(OMe)_3$), 6.10 (1 H, br. s, *H*N-SO_2), 4.24 (1 H, d, *J* 7.5, CH), 3.93 (3 H, s, *p*-*(*O*CH*$_3$*)*), 3.86 - 3.90 (1 H, m), 3.78 (6 H, s, *m*-(O*CH*$_3$)$_2$), 3.57 - 3.65 (2 H, m, N-CH*H*-Ar and CH), 3.39 (1 H, d, *J* 12.8, N-CH*H*-Ar), 1.51 (1 H, br. s., CH-N*H*-CH_2); δ_C (126 MHz, $CDCl_3$): 152.91, 141.90, 139.78, 138.49, 137.76, 137.52, 137.03, 136.74, 136.58, 130.16, 129.85, 129.41, 128.66, 128.42, 128.34, 128.02, 127.81, 127.77, 127.71, 127.66, 127.60, 127.43, 127.27, 127.10, 107.38, 106.33, 105.98, 99.31, 77.26, 76.74, 67.27, 63.33, 62.99, 60.93, 56.24, 56.12, 49.09; m/z (ESI+): 735.1 ($[M + H]^+$, 100%), 757.1 ($[M+Na]^+$, 34%).

N-((*R*,*R*)-2- ((4'-methoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide ruthenium (II) chloride complex **14**.



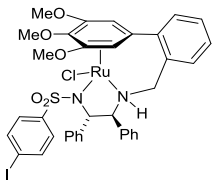
(*R*,*R*)-2-((4'-methoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide **17** (0.402g, 0.60 mmol, 1 eq.), [Ru ($C_6H_5CO_2Et$)Cl_2]$_2$ (0.193g, 0.30 mmol, 0.5 eq) and 4Å-MS (0.315g) were added together in dry chlorobenzene (15 mL). The reaction mixture was degassed, heated rapidly to 91°C in a preheated aluminium block and stirred for 22 h, followed by mass spectrometry, before the chlorobenzene was removed under vacuum. The product was filtered through celite and a silica plug in 10% IPA/CHCl3. The crude product was purified by column chromatography on silica (31g silica, first elution using 5-10% EtOAc: 25-20% Hexane: 70% DCM to remove the excess ligand and then gradient elution 2-20% MeOH: 28-10% Hexane: 70% DCM) to give the product (*R*,*R*)-**14** as a brown powder (0.268g, 0.33 mmol, 55.7%). Mp 287.5°C (dec); $[\alpha]^D$ 155.7 (c 0.004 in $CHCl_3$); HRMS: found (ESI): $[M + H]^+$ 775.0081 ($C_{34}H_{30}IN_2O_3RuS$ requires 775.0068); ν_{max}: 3462, 3435, 3057, 3027, 2932, 2835, 1541, 1453, 1248, 1134, 1080, 1002, 898, 805, 761, 723, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm: 7.64 (1 H, d, *J* 6.9, ArH), 7.58 (1 H, t, *J* 7.5, ArH), 7.43 (1 H, td, *J* 7.5, 1.0, ArH), 7.35 (2 H, d, *J* 8.4, *o*-I-ArH), 6.97 - 7.20 (7 H, m, ArH and *o*-SO_2-ArH), 6.77 (1 H, t, *J* 7.3, ArH), 6.60 (3 H, t, *J* 7.7, ArH), 6.38 (2 H, d, *J* 7.3, ArH), 6.33 (1 H, dd, *J* 5.8, 1.4, Ru-ArH), 5.89 (1 H, dd, *J* 6.6, 1.4, Ru-ArH), 5.40 (1 H, d, *J* 5.8, Ru-ArH), 5.18 (1 H, d, *J* 6.4, Ru-ArH), 4.87 (1 H, d, *J* 12.2, N*H*), 4.61 (1 H, dd, *J* 14.1, 2.4, ArHC*H*-N), 4.19 (3 H, s, OCH_3), 4.11 (1 H, d, *J* 11.1, N-C*H*), 3.70 - 3.94 (1 H, m, ArHC*H*-N), 3.11 (1 H, t, *J* 11.7, N-C*H*); δ_C (126 MHz, CDCl3): 145.10, 138.07, 136.41, 135.67, 134.19, 132.43, 131.98, 130.87, 130.40, 130.08, 129.77, 129.40, 129.05, 128.95, 128.73, 128.57, 127.48, 126.84, 126.49, 95.81, 88.64, 81.31, 80.18, 77.26, 76.80, 76.75, 76.67, 75.36, 68.86, 57.38, 53.87; m/z (ESI+): 774.9 ($[M - Cl]^+$, 100%).

N-((*S*,*S*)-2- ((3',5'-dimethoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide ruthenium (II) chloride complex **15**



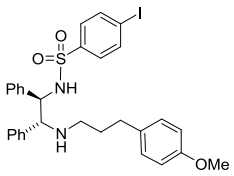
(S,S)-(3',5'-Dimethoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide **18** (0.291g, 0.41 mmol, 1 eq.), [Ru ($C_6H_5CO_2Et$)Cl_2]$_2$ (0.137g, 0.21 mmol, 0.51 eq) and 4Å-MS (0.228g) were added together in dry chlorobenzene (10 mL). The reaction mixture was degassed, heated rapidly to 90°C in a preheated aluminium block and stirred for 23 h, followed by mass spectrometry, before the chlorobenzene was removed under vacuum. The product was filtered through celite and a silica plug in 10% IPA/$CHCl_3$. The crude product was purified by column chromatography on silica (30.8g silica, first elution using 5-10% EtOA: 25-20 % Hexane: 70% DCM to remove the excess ligand and then gradient elution 5-20% MeOH: 25-10% Hexane: 70% DCM) to give the product *(S,S)*-**15** as a brown powder (0.154g, 0.18 mmol, 44.4%). $[\alpha]^D$ 152.1 (c 0.002 in $CHCl_3$); HRMS: found (ESI): $[M + H]^+$ 805.0177 ($C_{35}H_{32}IN_2O_4RuS$ requires 805.0166); ν_{max}: 3183, 3075, 3060, 3027, 2931, 2333, 2291, 1729, 1591, 1568, 1525, 1493, 1454, 1346, 1266, 1204, 1157, 1134, 1080, 1005, 901, 810, 761, 723, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm: 7.63 (1 H, d, *J* 7.5, ArH), 7.54 (1 H, t, *J* 7.5, ArH), 7.29 - 7.38 (4 H, m, ArH), 7.22 - 7.28 (4 H, m, ArH), 6.99 - 7.22 (5 H, m, ArH), 6.73 - 6.83 (3 H, m, ArH), 6.66 (2 H, t, *J* 7.6, ArH), 6.50 (2 H, d, *J* 7.3, ArH), 5.58 (1 H, s, Ru-*H*-Ar-*o*- $(OMe)_2$), 4.78 - 4.87 (2 H, m, Ru-ArH and N*H*), 4.58 (1 H, dd, *J* 13.9, 1.8, ArHC*H*-N), 4.55 (1 H, s, Ru-ArH), 4.13 (3 H, s, OCH_3), 4.10 (3 H, s, OCH_3), 3.68 - 3.79 (2 H, m, ArHC*H*-N and N-C*H*), 3.36 (1 H, t, *J* 11.7, N-C*H*); δ_C (126 MHz, $CDCl_3$): 144.82, 141.35, 138.71, 137.54, 137.44, 136.20, 135.37, 133.69, 132.43, 131.37, 130.00, 129.87, 129.69, 129.55, 128.90, 128.68, 128.51, 127.12, 126.42, 107.25, 106.96, 99.97, 96.07, 95.96, 94.56, 79.61, 77.28, 77.02, 76.77, 76.45, 68.90, 60.70, 57.81, 57.78, 57.19, 55.38, 52.47, 52.06; m/z (ESI+): 805.0 ($[M - Cl]^+$, 100%).

N- ((*S*,*S*)-2- ((3',4',5'-trimethoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide ruthenium (II) chloride complex **16**



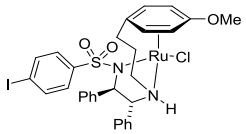
(S,S)-2-((3',4',5'-Trimethoxy-[1,1'-biphenyl]-2-ylmethyl)amino)-1,2-diphenylethyl)-4-iodobenzenesulfonamide **19** (0.296g, 0.40mmol, 1 eq.), $[Ru(C_6H_5CO_2Et)Cl_2]_2$ (0.13g, 0.20 mmol, 0.5 eq) and 4Å-MS (0.210g) were added together in dry chlorobenzene (10 mL). The reaction mixture was degassed, heated rapidly to 90°C in a preheated aluminium block and stirred for 23 h, followed by mass spectrometry, before the chlorobenzene was removed under vacuum. The product was filtered through celite and a silica plug in 10% IPA/$CHCl_3$. The crude product was purified by column chromatography on silica (30.1g silica, first elution using 5-15% EtOAC: 25-15 % Hexane: 70% DCM to remove the excess ligand and then gradient elution 5-15% MeOH: 25-15% Hexane: 70% DCM) to give the product *(S,S)*-**16** as a brown powder (0.184g, 0.21 mmol, 52.5%). HRMS: found (ESI): $[M + H]^+$ 835.0291 ($C_{36}H_{34}IN_2O_5RuS$ requires 835.0280); ν_{max}: 3524, 3510, 3446, 3180, 3057, 33026, 2931, 1729, 1568, 1454, 1419, 1346, 1223, 1111, 1003, 901, 808, 723, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) δ ppm: 7.65 (1 H, d, *J* 6.7, ArH), 7.50 - 7.60 (2 H, m, ArH), 7.33 - 7.44 (4 H, m, ArH), 7.30 (3 H, m, *J* 8.7, ArH), 7.18 (2 H, m, *J* 6.8, ArH), 6.83 - 6.90 (1 H, m, ArH), 6.80 (1 H, d, *J* 7.3, ArH), 6.74 (2 H, t, *J* 7.4, ArH), 6.46 (2 H, d, *J* 7.1, ArH), 4.87 (1 H, s, Ru-ArH), 4.70 (1 H, d, *J* 11.4, NH), 4.61 (1 H, d, *J* 13.8, Ar-CH_2-N), 4.51 (3 H, br. s, OCH_3), 4.42 (1 H, br. s., Ru-ArH), 4.27 (3 H, br. s, OCH_3), 4.00 (4 H, br. s , OCH_3 and NC*H*), 3.73 (2 H, m, *J* 13.7, Ar-CH_2-N), 3.30 (1 H, t, *J* 11.6, N-C*H*); δ_C (126 MHz, $CDCl_3$): 143.72, 139.62, 136.23, 135.37, 134.94, 133.72, 132.11, 131.47, 130.25, 130.19, 129.84, 129.69, 128.64, 128.40, 127.15, 126.70, 106.72, 106.18, 96.38, 91.39, 77.26, 76.75, 76.31, 69.25, 64.41, 60.92, 60.37, 59.19, 57.64, 57.20, 56.25, 54.87, 52.72; m/z (ESI+): 835.0 ($[M - Cl]^+$, 100%).

4-Iodo-*N*- ((*R*,*R*)-2-(3-(4-methoxyphenyl)propylamino)-1,2-diphenylethyl)benzenesulfonamide **25.**



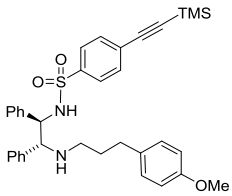
To a mixture of 3-(4-methoxyphenyl)propanol (0.278 g, 1.67 mmol, 1.6 eq) and 2,6-lutidine (0.255 mL, 2.197 mmol, 2.10 eq) in dry DCM (10 mL) was added a solution of triflic anhydride (1M in DCM) (1.78 mL, 1.778 mmol, 1.70 eq) dropwise at 0 ^{o}C under an inert atmosphere. The resulting light pink solution was stirred at 0 ^{o}C for 30 min and at room temperature for 60 min. The mixture was again cooled to 0 ^{o}C. To this, a solution of (*S*,*S*)-*N*-2-amino-1,2-diphenylethyl)-4-iodobenzenesulfonamide (0.500 g, 1.046 mmol, 1.0 eq) and TEA (0.349 mL, 2.510 mmol, 2.4 eq) in dry DCM (5 mL) was added dropwise at 0 ^{o}C. The resulting yellow coloured mixture was stirred at 0 ^{o}C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (15 mL) and washed with sat. $NaHCO_3$ solution (3 x 10 mL).The organic layer was separated, washed with H_2O (2 x 10 mL), brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to give the crude compound. The crude compound was purified by column chromatography on silica gel using EtOAc: Pet. ether (30:70) as an eluent to give a product. The product was triturated in n-pentane (to remove traces of 2,6-lutidine). The solvent was evaporated to give the pure compound (*S,S)*-**25** as white solid (0.439 g, 0.701 mmol, 67%). Mp 122-124 ^{o}C; $[\alpha]_D^{28}$ = +8.7 (*c* 0.505 in $CHCl_3$); HRMS found 627.1174 ($C_{30}H_{31}IN_2O_3S$ H+ requires 627.1173, error = -0.1 ppm); ν_{max} 3305, 3028, 2997, 2926, 2831, 1611, 1567, 1510, 1493, 1459, 1161, 811, 727, 701 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.52 (2H, d, *J* 8.4, -C*H* of -$SO_2C_6H_4I$), 7.18-7.04 (8H, m, ArH, -C*H* of -$SO_2C_6H_4I$), 6.98 (2H, d, *J* 8.8, -C*H* of -$C_6H_4(OCH_3)$), 6.96-6.91 (4H, m, ArH), 6.79 (2H, d, *J* 8.8, -C*H* of -C_6H_4 (OCH_3)), 6.33 (1H, br s, -N*H*Ts), 4.30 (1H, d, *J* 7.4, -C*H*NHTs), 3.78 (3H, s, -OC*H*$_3$), 3.61 (1H, d, *J* 7.4, -C*H*NH $(CH_2)_3$-), 2.53-2.40 (3H, m, -NH-C*H*HCH$_2$C*H*$_2$-), 2.31-2.26 (1H, m, -NH-CH*H*CH$_2$CH$_2$-), 1.74-1.59 (2H, m, -NH-CH$_2$C*H*$_2$CH$_2$-), 1.28 (1H, br s, -N*H* $(CH_2)_3$-); δc (100 MHz, $CDCl_3$) 157.75 (C), 139.83 (C), 139.05 (C), 137.94 (C), 137.56 (2CH), 133.70 (C), 129.17 (2CH), 128.38 (4CH), 128.08 (2CH), 127.57 (CH), 127.48 (3CH), 127.24 (2CH), 113.75 (2CH), 99.29 (C), 67.49 (CH), 63.09 (CH), 55.24 (OCH_3), 46.40 (CH_2), 32.32 (CH_2), 31.60 (CH_2); m/z ESI-MS $[M+H]^+$ 627.1.

{4-Iodo-*N*-((*R*,*R*)-2-(3-(4-methoxyphenyl)propylamino)-1,2-diphenylethyl)benzenesulfonamide} -ruthenium chloride **22.**



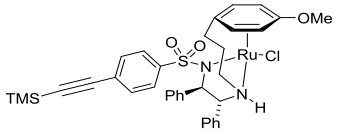
(*R,R)*-2-(3-(4-methoxyphenyl)propylamino)-1,2-diphenylethyl)benzenesulfonamide **25** (0.300 g, 0.479 mmol, 1.0 eq) and $[(C_6H_5CO_2Et)RuCl_2]_2$ (0.154 g, 0.150 mmol, 0.5 eq) were dissolved in dry DCM (15 mL) under N_2 and stirred at room temp for 30 min to give a brick red solution. The mixture was concentrated on a rotary evaporator to give a dark orange residue. To this, chlorobenzene (30 mL) was added and mixture heated at 90 ^oC for 5 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The solid was scratched in diethyl ether, filtered and dried to give dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 86:14) to give compound as a brown solid. The solid was recrystallized from MeOH to give pure product (*R,R)*-**22** as an orange solid (0.125 g, 0.164 mmol, 34%). Mp decomposition >280 ^oC; $[\alpha]_D^{28}$ = -164.54 (*c* 0.055 in $CHCl_3$); HRMS found 727.0072 ($C_{30}H_{30}N_2O_3RuS$-Cl+ requires 727.0067, error = -1.4 ppm). ν_{max} 3198, 3051, 3027, 2925, 2872, 1572, 1533, 1509, 1465, 1454, 1279, 1266, 1255, 835, 796, 725, 694 cm^{-1}; δ_H (500 MHz, CD_2Cl_2) 7.34 (2H, d, *J* 8.3, -C*H* of -$SO_2C_6H_4I$), 7.23-7.16 (3H, m, ArH), 7.10 (2H, d, *J* 8.3, -C*H* of -$SO_2C_6H_4I$), 6.96-6.86 (3H, m, ArH), 6.73-6.70 (2H, m, ArH), 6.60 (2H, d, *J* 7.5, ArH), 5.55 (1H, d, *J* 5.8, -C*H* of Ru-Ar), 5.51 (1H, d, *J* 5.8, -C*H* of Ru-Ar), 5.37 (1H, d, *J* 6.0, -C*H* of Ru-Ar), 5.31 (1H, d, *J* 6.0, -C*H* of Ru-Ar), 4.27 (1H, d, *J* 11.0, -C*H*NTs), 4.00-3.96 (1H, m, -N*H* $(CH_2)_3$-), 3.96 (3H, s, -OCH_3), 3.68-3.63 (1H, m, -C*H*NH $(CH_2)_3$-), 2.80-2.75 (1H, m, -NH-C*H*HCH$_2$CH$_2$-), 2.53-2.44 (2H, m, -NH-CH*H*CH$_2$C*H*H-), 2.34-2.29 (1H, m, -NH-CH$_2$CH$_2$CH*H*-), 2.16-2.10 (1H, m, -NH-CH$_2$C*H*HCH_2-), 2.02-1.93 (1H, m, -NH-CH$_2$CH*H*CH_2-); δc (125 MHz, CD_2Cl_2) 147.61 (C), 138.96 (C), 136.87 (2CH), 136.80 (C), 135.27 (C), 129.45 (2CH), 129.21 (CH), 129.09 (4CH), 128.96 (CH), 127.64 (2CH), 126.83 (2CH), 95.45 (C), 91.85 (C), 85.34 (CH), 81.68 (CH), 79.63 (CH), 72.19 (CH), 69.13 (CH), 65.75 (CH), 57.19 (OCH_3), 50.08 (CH_2), 31.09 (CH_2), 27.63 (CH_2); m/z ESI-MS $[M-Cl]^+$ 727.0.

N-((*R*,*R*)-2-(3-(4-Methoxyphenyl)propylamino)-1,2-diphenylethyl)-4-(2-(trimethylsilyl)ethynyl)benzenesulfonamide **26.**



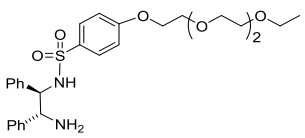
In glass tube, diamine (*R,R*)- 4-Iodo-*N*- ((*R,R*)-2-(3-(4-methoxyphenyl)propylamino)-1,2-diphenylethyl)benzenesulfonamide **25** (0.501 g, 0.8 mmol, 1.0 eq), $PdCl_2$ $(PPh_3)_4$ (28 mg, 0.040 mmol, 0.05 eq) and CuI (15.3 mg, 0.080 mmol, 0.1 eq) were dissolved in dry THF (10 mL) under an inert atmosphere followed by TEA (2.5 mL). The resulting mixture was stirred for 5 min followed by addition of trimethylsilylacetylene (0.382 mL, 2.71 mmol, 3.89 eq). The glass tube was sealed under an inert atmosphere and stirred at room temperature for 22h. The reaction mixture was filtered through Celite and washed with EtOAc (2 x 20 mL). The filtrate was concentrated on a rotary evaporator to give a residue. The crude compound was purified by column chromatography over silica gel using EtOAc: Pet. ether (26:74) as an eluent to give the pure product (*R,R*)-**26** as a light green solid (0.426 g, 0.714 mmol, 89%). Mp 48-50^oC; $[\alpha]_D^{28}$ = +9.29 (*c* 0.280 in $CHCl_3$); ν_{max} 3263, 3060, 3030, 2931, 2834, 2159, 1611, 1590, 1510, 1453, 1395, 1244, 1153, 838, 758, 697 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.37 (2H, d, *J* 8.4, -C*H* of -$SO_2C_6H_4$-), 7.28 (2H, d, *J* 8.4, -C*H* of -$SO_2C_6H_4$-), 7.15-7.02 (6H, m, ArH), 6.99 (2H, d, *J* 8.4, -C*H* of -C_6H_4 (OCH_3)), 6.95-6.89 (4H, m, ArH), 6.80 (2H, d, *J* 8.4, -C*H* of -$C_6H_4(OCH_3)$), 6.37 (1H, br s, -N*H*Ts), 4.27 (1H, d, *J* 8.0, -C*H*NHTs), 3.78 (3H, s, -OCH_3), 3.59 (1H, d, *J* 8.0, -C*H*NH $(CH_2)_3$-), 2.55-2.40 (3H, m, -NH-C*H*HCH_2CH_2-), 2.32-2.26 (1H, m, -NH-CH*H*CH_2CH_2-), 1.75-1.61 (2H, m, -NH-CH_2CH_2CH_2-), 1.37 (1H, br s, -N*H* $(CH_2)_3$-), 0.26 (9H, s, -Si $(CH_3)_3$); δc (100 MHz, $CDCl_3$) 157.75 (C), 139.59 (C), 139.06 (C), 137.96 (C), 133.72 (C), 131.82 (2CH), 129.18 (2CH), 128.37 (2CH), 128.01 (2CH), 127.58 (CH), 127.53 (2CH), 127.50 (CH), 127.28 (2CH), 127.01 (CH), 126.83 (2CH), 113.76 (2CH), 103.38 (C), 97.76 (C), 67.71 (CH), 63.31 (CH), 55.23 (OCH_3), 46.42 (CH_2), 32.33 (CH_2), 31.63 (CH_2), -0.194 (Si $(CH_3)_3$); m/z ESI-MS $[M+H]^+$ 597.2.

<u>{*N*-((*R,R*)-2-(3-(4-Methoxyphenyl)propylamino)-1,2-diphenylethyl)-4- (2-(trimethylsilyl)ethynyl)benzenesulfonamide} -ruthenium chloride **23.**</u>



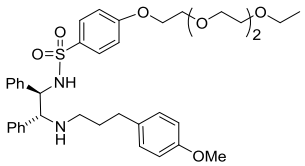
(*R*,*R*)-2-(3-(4-Methoxyphenyl)propylamino)-1,2-diphenylethyl)-4-(2-(trimethylsilyl)ethynyl)benzenesulfonamide **26** (0.373 g, 0.626 mmol, 1.0 eq) and [($C_6H_5CO_2Et$)$RuCl_2$]$_2$ (0.202 g, 0.313 mmol, 0.5 eq) were dissolved in dry DCM (15 mL) under N_2 and stirred at room temp for 30 min to give a brick red solution. The mixture was concentrated on a rotvapor to give a dark orange residue. To this, chlorobenzene (30 mL) was added and mixture heated at 90 ^oC for 5.5 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The solid was scratched in diethyl ether, filtered and dried to give dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 86:14) to give the crude compound as a brown solid. The solid was recrystallized from MeOH to give pure complex (*R*,*R*)-**23** as orange solid (0.094 g, 0.128 mmol, 20%). Mp decomposition >280 ^oC; $[\alpha]_D^{28}$ = -328.33 (*c* 0.03 in $CHCl_3$); HRMS found 697.1494 ($C_{35}H_{39}N_2O_3RuSSi$-Cl+ requires 697.1497, error = -0.1 ppm); ν_{max} 3190, 3051, 2936, 2917, 2156, 1533, 1465, 1454, 1257, 1181, 1041, 839, 814, 799, 760, 696 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.31 (2H, d, *J* 8.2, -C*H* of -$SO_2C_6H_4$-), 7.16-7.07 (3H, m, ArH), 7.03 (2H, d, *J* 8.4, -C*H* of -$SO_2C_6H_4$-), 6.83-6.79 (3H, m, ArH), 6.68-6.64 (2H, m, ArH), 6.55 (2H, d, *J* 7.6, ArH), 5.55 (1H, d, *J* 5.6, -C*H* of Ru-Ar), 5.48 (1H, d, *J* 5.6, -C*H* of Ru-Ar), 5.32 (1H, d, *J* 6.0, -C*H* of Ru-Ar), 5.28 (1H, d, *J* 6.0, -C*H* of Ru-Ar), 4.30 (1H, d, *J* 11.2, -C*H*NTs), 4.06-3.99 (1H, m, -N*H* $(CH_2)_3$-), 3.96 (3H, s, -OC*H*$_3$), 3.62-3.56 (1H, m, -C*H*NH $(CH_2)_3$-), 2.81-2.75 (1H, m, -NH-C*H*HCH_2CH_2-), 2.52-2.42 (1H, m, -NH-CH*H* CH_2CH_2-), 2.24-2.48 (1H, m, -NH-CH_2CH_2CH*H*-), 2.34-2.26 (1H, m, -NH-CH_2CH_2C*H*H-), 2.13-1.95 (2H, m, -NH-CH_2C*H*$_2CH_2$-), 0.24 (9H, s, -Si $(CH_3)_3$); δc (100 MHz, $CDCl_3$) 146.67 (C), 138.45 (C), 136.21 (C), 134.65 (C), 130.72 (4CH), 128.72 (4CH), 128.41 (CH), 127.05 (2CH), 126.80 (2CH), 126.45 (CH), 123.15 (C), 104.97 (C), 96.68 (C), 91.18 (C), 84.62 (CH), 81.33 (CH), 78.79 (CH), 72.03 (CH), 68.84 (CH), 65.46 (CH), 56.80 (OCH_3), 49.43 (CH_2), 30.34 (CH_2), 27.27 (CH_2), -0.006 (Si $(CH_3)_3$); m/z ESI-MS $[M-Cl]^+$ 697.1.

<u>*(R,R)*-4-(2-(2-(2-Ethoxyethoxy)ethoxy)ethoxy)-*N*-1,2-diphenylethyl)-benzenesulfonamide</u>



To a mixture of (*R,R*)-DPEN (0.637 g, 3.00 mmol) and TEA (0.760 mL, 5.460 mmol, 1.82 eq) in dry DCM (20 mL) was added a solution of chloride $C_{14}H_{21}ClO_6S$ (1.056 g, 3.00 mmol, 1.0 eq) in dry DCM (10 mL) dropwise at 0 ^oC under an inert atmosphere. The resulting light pink solution was stirred at 0 ^oC for 30 min and at room temperature for 18h. The mixture was concentrated on a rotary evaporator to give a crude compound. The crude compound was purified by column chromatography over silica gel using DCM:MeOH (95:5) as an eluent to give the pure product as an oil (1.380 g, 2.614 mmol, 87%). $[\alpha]_D^{28}$ = -11.15 (*c* 0.740 in $CHCl_3$); HRMS found 529.2354 ($C_{28}H_{36}N_2O_6S$ H+ requires 529.2367, error = 1.6 ppm); ν_{max} 3280, 3062, 3030, 2972, 2868, 1594, 1580, 1495, 1453, 1323, 1301, 1255, 1179, 1094, 1054, 923, 832, 766, 698 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.34 (2H, d, *J* 8.8, -C*H* of -$SO_2C_6H_4$-), 7.18-7.14 (6H, m, ArH), 7.11-7.09 (4H, m, ArH), 6.67 (2H, d, *J* 8.8, -C*H* of -$SO_2C_6H_4$-), 6.01 (1H, br s, -N*H*Ts), 4.35 (1H, d, *J* 5.6, -C*H*NHTs), 4.11-4.08 (3H, m, -C*H*NH_2, -C_6H_4-OC*H*$_2$$CH_2O$-), 3.85 (2H, t, *J* 4.8, -C_6H_4-OCH_2C*H*$_2$O-), 3.75-3.72 (2H, m, -OC*H*$_2$$CH_2O$-$CH_2CH_2OEt$), 3.70-3.68 (2H, m, -$OCH_2$C*H*$_2$$OCH_2CH_2OEt$), 3.67-3.64 (2H, m, -$OCH_2CH_2$OC*H*$_2$$CH_2OEt$), 3.61-3.57 (2H, m, -$OCH_2CH_2OCH_2$C*H*$_2$OEt), 3.52 (2H, q, *J* 7.1, -OC*H*$_2$$CH_3$), 1.51 (2H, br s, -N*H*$_2$), 1.20 (3H, t, *J* 7.1, -OCH_2C*H*$_3$); δc (100 MHz, $CDCl_3$) 161.49 (C), 141.46 (C), 139.18 (C), 131.93 (C), 128.86 (2CH), 128.41 (2CH), 128.21 (2CH), 127.51 (CH), 127.37 (CH), 127.01 (2CH), 126.51 (2CH), 114.25 (2CH), 70.88 (CH_2), 70.72 (CH_2), 70.63 (CH_2), 69.79 (CH_2), 69.41 (CH_2), 67.66 (CH_2), 66.61 (CH_2), 63.15 (CH), 60.52 (CH), 15.13 (CH_3); m/z ESI-MS $[M+H]^+$ 529.2.

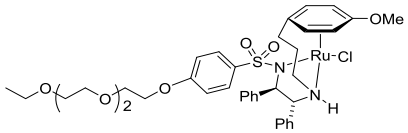
<u>*(R,R)*-4-(2-(2-(2-Ethoxyethoxy)ethoxy)ethoxy)-*N*-2-(3-(4-methoxyphenyl)-propylamino)-1,2-diphenylethyl)benzenesulfonamide **27.**</u>



To a mixture of alcohol 3-(4-methoxyphenyl)propanol (0.266 g, 1.60 mmol, 1.6 eq) and 2,6-lutidine (0.245 mL, 2.10 mmol, 2.10 eq) in dry DCM (15 mL) was added a solution of triflic anhydride (1M in DCM) (1.7 mL, 1.70 mmol, 1.70 eq) dropwise at 0 ^oC under an inert atmosphere. The resulting light pink solution was stirred at 0 ^oC for 30 min and at room temperature for 60 min. The mixture was again cooled down to 0 ^oC. To this, a solution of (*R,R*)-4-(2-(2-(2-ethoxyethoxy)ethoxy)ethoxy)-N-1,2-diphenylethyl)-

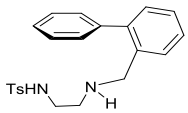
benzenesulfonamide (0.560 g, 1.0 mmol, 1.0 eq) and TEA (0.334 mL, 2.40 mmol, 2.4 eq) in dry DCM (10 mL) was added dropwise at 0 ^{o}C. The resulting yellow coloured mixture was stirred at 0 ^{o}C for 30 min and then at room temperature for 17 h. The reaction mixture was diluted with DCM (20 mL) and washed with sat. $NaHCO_3$ solution (3 x 20 mL).The organic layer was separated, washed with H_2O (2 x 20 mL), brine (15 mL), dried over anhydrous Na_2SO_4, filtered and concentrated to give crude compound. The crude compound was purified by column chromatography over silica gel using EtOAc: Pet. ether (70:30) as an eluent to give a residue. The residue was triturated in n-pentane (to remove traces of 2,6-lutidine) but there was no any solid separation. The solvent was evaporated to give pure compound (*R,R*)-**27** as an oil (0.510 g, 0.754 mmol, 75%). $[\alpha]_D^{28}$ = -11.9 (*c* 0.470 in $CHCl_3$); HRMS found 677.3254 ($C_{38}H_{48}N_2O_7S$ H+ requires 677.3255, error = 0.3 ppm); ν_{max} 3262, 5062, 3029, 2864, 1594, 1580, 1511, 1495, 1453, 1300, 1244, 1149, 1093, 1030, 924, 830, 770, 698 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.39 (2H, d, *J* 8.8, -C*H* of -$SO_2C_6H_4$-), 7.15-7.12 (3H, m, ArH), 7.06-7.02 (3H, m, ArH), 7.00 (2H, d, *J* 8.6, -C*H* of -$C_6H_4OCH_3$), 6.94-6.88 (4H, m, ArH), 6.80 (2H, d, *J* 8.6, -C*H* of -$C_6H_4OCH_3$), 6.70 (2H, d, *J* 8.8, -C*H* of -$SO_2.C_6H_4$-), 6.26 (1H, br s, -N*H*Ts), 4.22 (1H, d, *J* 8.0, -C*H*NHTs), 4.11-4.08 (2H, m, -C_6H_4-OC*H*$_2CH_2O$-), 3.85 (2H, t, *J* 5.0, -C_6H_4-OCH_2CH_2O-), 3.78 (3H, s, -OC*H*$_3$), 3.74-3.72 (2H, m, -OC*H*$_2CH_2OCH_2CH_2OEt$), 3.70-3.68 (2H, m, -OCH_2C*H*$_2OCH_2CH_2OEt$), 3.67-3.64 (2H, m, -OCH_2CH_2OC*H*$_2CH_2OEt$), 3.60-3.56 (3H, m, -C*H*NH $(CH_2)_3$-, -$OCH_2CH_2OCH_2$C*H*$_2$OEt), 3.52 (2H, q, *J* 7.2, -OC*H*$_2CH_3$), 2.54-2.40 (3H, m, -NH-C*H*HCH$_2$C*H*$_2$-), 2.32-2.25 (1H, m, -NH-CH*H*CH$_2CH_2$-), 1.73-1.61 (2H, m, -NH-CH_2C*H*$_2CH_2$-), 1.45 (1H, br s, -N*H* $(CH_2)_3$-), 1.20 (3H, t, *J* 7.2, -OCH_2C*H*$_3$); δc (100 MHz, $CDCl_3$) 161.59 (C), 157.72 (C), 139.26 (C), 138.26 (C), 133.78 (C), 131.86 (C), 129.17 (2CH), 129.12 (2CH), 128.28 (2CH), 127.90 (2CH), 127.55 (2CH), 127.46 (CH), 127.35 (2CH), 127.28 (CH), 114.20 (2CH), 113.73 (2CH), 70.88 (CH_2), 70.71 (CH_2), 70.62 (CH_2), 69.79 (CH_2), 69.41 (CH_2), 67.73 (CH), 67.68 (CH_2), 66.61 (CH_2), 63.04 (CH), 55.22 (OCH_3), 46.42 (CH_2), 32.33 (CH_2), 31.68 (CH_2), 15.13 (CH_3); m/z ESI-MS $[M+H]^+$ 677.3.

(R,R)-{4-(2-(2-(2-Ethoxyethoxy)ethoxy)ethoxy)-*N*-*(*2-(3-(4-methoxyphenyl)-propylamino)-1,2-diphenylethyl)benzenesulfonamide}-ruthenium chloride **24.**



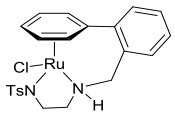
(R,R)-4-(2-(2-(2-Ethoxyethoxy)ethoxy)ethoxy)-*N*-2-(3-(4-methoxyphenyl)-propylamino)-1,2-diphenylethyl)benzenesulfonamide **27** (0.203 g, 0.300 mmol, 1.0 eq) and $[(C_6H_5CO_2Et)RuCl_2]_2$ (0.097 g, 0.150 mmol, 0.5 eq) were dissolved in dry DCM (15 mL) under N_2 and stirred at room temp for 30 min to give a brick red solution. The mixture was concentrated on a rotary evaporator to give a dark orange residue. To this, chlorobenzene (20 mL) was added and the mixture was heated at 90 ^oC for 6 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The solid was scratched in diethyl ether, filtered and dried to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (97:3 to 86:14) to give (*R,R*)-**24** as a brown solid. The solid was recrystallized from MeOH to give pure complex as orange brown solid (0.075 g, 0.092 mmol, 30%). Mp decomposition >180 ^oC; $[\alpha]_D^{29}$ = + 646.7 (*c* 0.003 in $CHCl_3$); HRMS found 777.2163 ($C_{38}H_{47}N_2O_7RuS$-Cl+ requires 777.2151, error = -2.0 ppm); ν_{max} 3191, 3059, 3027, 2865, 1725, 1594, 1536, 1510, 1494, 1453, 1248, 1124, 1081, 1038, 1011, 938, 906, 815, 801. 698cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.31 (2H, d, *J* 8.6, -C*H* of -$SO_2C_6H_4$-), 7.17-7.06 (3H, m, ArH), 6.85-6.74 (3H, m, ArH), 6.68-6.64 (2H, m, -ArH), 6.55 (2H, d, *J* 7.2, ArH), 6.46 (2H, d, *J* 8.6, -C*H* of -$SO_2C_6H_4$-), 5.55 (1H, d, *J* 4.2, -C*H* of Ru-Ar), 5.47 (1H, d, *J* 4.2, -C*H* of Ru-Ar), 5.34 (1H, d, *J* 5.4, -C*H* of Ru-Ar), 5.26 (1H, d, *J* 5.4, -C*H* of Ru-Ar), 4.30 (1H, d, *J* 10.8, -C*H*NTs), 4.06-3.94 (6H, m, -C_6H_4-OC*H*$_2$$CH_2O$-, -OC*H*$_3$, -N*H* $(CH_2)_3$-), 3.81 (2H, t, *J* 4.8, -C_6H_4-OCH_2C*H*$_2$O-), 3.72-3.65 (6H, m, -OC*H*$_2$C*H*$_2$OC*H*$_2$$CH_2OEt$), 3.61-3.57 (2H, m, -$OCH_2CH_2OCH_2$C*H*$_2$OEt, -C*H*NH $(CH_2)_3$-), 3.52 (2H, q, *J* 7.0, -OC*H*$_2$$CH_3$), 2.82-2.72 (1H, m, -NH-C*H*HCH_2CH_2-), 2.51-2.37 (2H, m, -NH-CH*H*CH_2C*H*H-), 2.33-2.27 (2H, m, -NH-CH_2CH_2CH*H*-), 2.17-1.96 (2H, m, -NH-CH_2C*H*$_2$$CH_2$-), 1.20 (3H, t, *J* 7.0, -OCH_2C*H*$_3$); δc (100 MHz, $CDCl_3$) 158.92 (C), 139.06 (C), 138.65 (C), 136.28 (C), 134.60 (C), 128.75 (2CH), 128.62 (6CH), 128.31 (CH), 126.92 (2CH), 126.16 (CH), 113.12 (2CH), 91.10 (C), 84.65 (CH), 81.49 (CH), 78.56 (CH), 72.15 (CH), 7.77 (CH_2), 70.66 (CH_2), 70.58 (CH_2), 69.76 (CH_2), 69.55 (CH_2), 68.91 (CH), 67.40 (CH_2), 66.59 (CH_2), 65.52 (CH), 56.76 (OCH_3), 49.36 (CH_2), 30.22 (CH_2), 27.30 (CH_2), 15.12 (CH_3); m/z ESI-MS $[M-Cl]^+$ 777.1.

N-(2-(Biphenyl-2-yl)methylamino)ethyl)-4-methylbenzenesulfonamide.



To biphenylcarboxaldehyde (182 mg, 1.00 mmol) was added activated molecular sieves (1 g) and anhydrous MeOH (6 mL). To this was added TsEN (246 mg, 1.10 mmol) and acetic acid (50 μL). The reaction was stirred at room temperature for 5 h and then $NaBH_3CN$ (251 mg, 4.00 mmol) was added and the reaction stirred at room temperature overnight. After this the reaction was filtered and the solid washed with DCM. The filtrate and DCM washings were combined and dried under reduced pressure. The residue was then dissolved in anhydrous DCM and washed with 1M NaOH (aq) solution. The DCM phase was separated, dried over Na_2SO_4, filtered and the solvent removed under reduced pressure to give the product as a pale yellow viscous oil (134 mg, 0.35 mmol, 70%). HRMS (found (ESI): M^+ + H, 381.1632 $C_{22}H_{25}N_2O_2S$ requires M, 381.1631); υ_{max} 3272, 2858, 1477, 1450, 1322, 1155, 1091, 814, 775, 750, 703 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.67 (2H, d *J* 8.1, SO_2CHAr), 7.43-7.11 (13H, m, ArH and N*H* overlapping), 3.58 (2H, s, $ArCH_2N$), 2.84 (2H, dd *J* 6.5 and 4.8, CH_2NHSO_2), 2.50 (2H, dd *J* 6.5 and 4.8, CH_2NH), 2.40 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 142.64 (*C*Ar), 141.24 (*C*Ar), 140.53 (*C*Ar), 136.39 (*C*Ar), 136.22 (*C*Ar), 129.57 (*C*HAr), 129.04 (2 *C*HAr), 128.50 (*C*HAr), 128.27 (2 *C*HAr), 127.68 (2 *C*HAr), 126.95 (*C*HAr), 126.62 (*C*HAr), 126.55 (*C*HAr), 126.49 (2 *C*HAr), 50.06 (CH_2), 46.65 (CH_2), 41.60 (CH_2), 20.92 (CH_3); *m/z* (ESI) 381.0 (M^+ + 1).

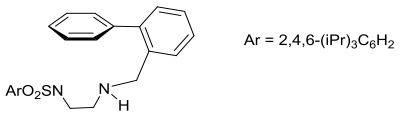
{*N*-([2-(biphenyl-2-yl)methylamino]ethyl-4-methylbenzenesulfonamide} ruthenium chloride **28.**



N-(2-(Biphenyl-2-yl)methylamino)ethyl)-4-methylbenzenesulfonamide (0.450 g, 1.184 mmol, 1.0 eq) and $[(C_6H_5CO_2Et)RuCl_2]_2$ (0.381g, 0.592 mmol, 0.5 eq) were dissolved in dry DCM (40 mL) under N_2 and stirred at room temp for 30 min to give a brick red solution. The mixture was concentrated on a rotary evaporator to give a dark orange residue. To this, chlorobenzene (60 mL) was added and mixture heated at 140 ^oC for 5.5 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The solid was scratched in diethyl ether, filtered and dried

to give a dark brown solid. The solid was purified by column chromatography over Florisil using DCM:MeOH (95:5 to 86:14) to give compound as a brown solid. The solid was recrystallized using a mixture of MeOH and Et_2O to give pure complex **28** as brown solid (0.105 g, 0.203 mmol, 14%). Mp decomposition >184 ^oC; HRMS found 481.0524 ($C_{22}H_{23}N_2O_2SRu$-Cl+ requires 481.0523, error = -0.7 ppm); ν_{max} 3059, 2922, 2855, 1596, 1480, 1439, 1260, 1182, 1129, 811, 747, 704, 659 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 7.74 (2H, d, *J* 6.9, *m*-C*H* of -$SO_2C_6H_4CH_3$), 7.52-7.40 (4H, m, ArH), 7.16 (2H, d, *J* 6.9, *o*-C*H* of -$SO_2C_6H_4CH_3$), 6.67 (1H, br s, -C*H* of Ru-Ar), 5.81 (1H, br s, -C*H* of Ru-Ar), 5.68 (1H, br s, -C*H* of Ru-Ar), 5.28 (1H, br s, -C*H* of Ru-Ar), 5.25 (1H, br s, -C*H* of Ru-Ar), 4.78 (1H, br d, -CH_2-NH-C*H*H-C_6H_4-), 4.49 (1H, br s, -CHN*H*-CH_2-), 4.28 (1H, br d, -CH_2-NH-CH*H*-C_6H_4-), 3.07 (1H, br d, -NHTs-C*H*H-), 2.59 (1H, br s, -C*H*H-NH-CH_2-C_6H_4-), 2.33 (4H, br s, -NHTs-CH*H*-, -CH_3), 2.14 (1H, br s, -CH*H*-NH-CH_2-C_6H_4-); δc (150 MHz, $CDCl_3$) 140.49 (C), 140.40 (C), 134.69 (C), 132.36 (C), 131.24 (CH), 129.81 (CH), 129.74 (CH), 129.37 (CH), 128.66 (2CH), 127.13 (2CH), 93.04 (C), 92.28 (CH), 90.62 (CH), 81.27 (CH), 78.90 (CH), 77.47 (CH), 57.75 (CH_2), 55.43 (CH_2), 48.25 (CH_2), 21.31 (CH_3); m/z ESI-MS $[M\text{-}Cl]^+$ 480.9.

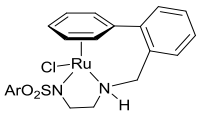
<u>*N*-[2-(Biphenyl-2-yl)methylamino]ethyl-2,4,6-triisopropylbenzenesulfonamide.</u>



To a mixture of *N*-2-(2,4,6-triisopropyl)benzenesulfonamido)ethylamine (0.500 g, 1.534 mmol, 1.10 eq) and MS 4A (0.6 g) in dry methanol (25 mL) was added biphenyl-2-carboxaldehyde (0.254 g, 1.395 mmol, 1.0 eq) followed by acetic acid (3-4 drops). The mixture was stirred at room temperature under an inert atmosphere for 4 h to form the imine. To this, $NaBH_3CN$ (0.351 g, 5.580 mmol, 4.0 eq) was added and the resulting mixture was stirred at room temperature for 18 h. The reaction mixture was filtered and concentrated to give a residue. This was dissolved in DCM (60 mL) and washed with 1M NaOH (2 x 25 mL), dried over anhydrous Na_2SO_4, filtered and evaporated on a rotary evaporator to give the crude product. The crude compound was purified by flash column chromatography over silica gel using EtOAc: Pet. ether (7:3) to give the product as an oil. The compound was solidified on standing overnight (0.643 g, 1.307 mmol, 93%). Mp 66-68 ^oC; HRMS found 493.2878 ($C_{30}H_{40}N_2O_2S$ H+ requires 493.2883, error = 1.0 ppm); ν_{max} 3277, 2961, 2930, 2869, 1599, 1456, 1424, 1333, 1320, 1301, 1163,

1154, 747, 699, 677 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.41-7.33 (4H, m, ArH), 7.32-7.27 (4H, m, -ArH), 7.24-7.20 (1H, m, ArH), 7.14 (2H, s, *m*-C*H* of -$SO_2C_6H_2$-), 4.95 (1H, br s, -N*H*SO_2-), 4.17-4.07 (2H, m, *o*-C*H*$(CH_3)_2$), 3.66 (2H, s, -NHC*H*$_2$-biphenyl), 2.94-2.85 (3H, m, *p*-C*H*$(CH_3)_2$, -SO_2NHC*H*$_2$C*H*$_2$NH-), 2.58-2.55 (2H, m, -SO_2NHCH_2C*H*$_2$NH-), 1.33 (1H, s, -SO_2NHCH_2CH_2N*H*-), 1.25 (6H, d, *J* 6.8, *p*-CH (C*H*$_3)_2$), 1.22 (12H, d, *J* 6.8, *o* -CH (C*H*$_3)_2$); δc (100 MHz, $CDCl_3$) 152.52 (C), 150.28 (2C), 141.76 (C), 141.06 (C), 136.95 (C), 132.12 (C), 130.11 (CH), 129.05 (CH), 128.81 (2CH), 128.24 (2CH), 127.47 (CH), 127.16 (CH), 127.10 (CH), 123.68 (2CH), 50.83 (CH_2), 47.29 (CH_2), 41.88 (CH_2), 34.10 (CH), 29.56 (2CH), 24.85 ($4CH_3$), 23.57 ($2CH_3$); m/z ESI-MS $[M+H]^+$ 493.2.

<u>{*N*-[2-(biphenyl-2-yl)methylamino]ethyl-2,4,6-triisopropylbenzenesulfonamide} ruthenium chloride **29.**</u>

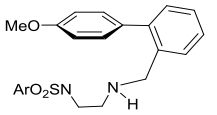


Ar = 2,4,6-$(iPr)_3C_6H_2$

N-[2-(Biphenyl-2-yl)methylamino]ethyl-2,4,6-triisopropylbenzenesulfonamide (0.500 g, 1.016 mmol, 1.0 eq) and $[(C_6H_5CO_2Et)RuCl_2]_2$ (0.327 g, 0.508 mmol, 0.5 eq) were dissolved in dry DCM (50 mL) under N_2 and stirred at room temp for 30 min to give a brick red solution. The mixture was concentrated on a rotary evaporator to give a dark orange residue. To this, chlorobenzene (150 mL) was added and mixture heated at 140 ^oC for 3.0 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The solid was purified by column chromatography over Florisil using EtOAc:MeOH:Pet.Ether (60:2:38 to 60:8:32) to give **29** as a brown solid. The solid was recrystallized using mixture of MeOH and Et_2O to give pure complex **29** as an orange solid (0.110 g, 0.175 mmol, 17%). Mp decomposition >280 ^oC; HRMS found 593.1776 ($C_{30}H_{39}N_2O_2SRu$-Cl+ requires 593.1777, error = -0.5 ppm); ν_{max} 3189, 2960, 2947, 2864, 1598,1455, 1437, 1267, 1246, 1123, 1055, 842, 816, 767, 748, 648 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.53-7.47 (2H, m, ArH), 7.46-7.42 (1H, m, ArH), 7.39-7.38 (1H, m, ArH), 7.07 (2H, s, *m*-C*H* of -$SO_2C_6H_2$-), 6.83 (1H, t, *J* 5.6,-C*H* of Ru-Ar), 6.03 (1H, t, *J* 5.6,-C*H* of Ru-Ar), 5.77 (1H, t, *J* 5.6,-C*H* of Ru-Ar), 5.39 (1H, d, *J* 5.6,-C*H* of Ru-Ar), 5.34 (1H, d, *J* 5.6,-C*H* of Ru-Ar), 4.64-4.60 (1H, m, -NHC*H*H-biphenyl), 4.52-4.42 (2H, m, *o*-C*H* $(CH_3)_2$), 4.40-4.31 (2H, m, -N*H*CH*H*-biphenyl), 2.90-2.83 (1H, m, *p*-C*H* $(CH_3)_2$), 2.73-2.70 (1H, m, -SO_2NHC*H*HCH_2NH-), 2.64-2.56

(2H, m, -SO_2NHCH*H*C*H*HNH-), 2.31-2.22 (1H, m, -SO_2NHCH_2CH*H*NH-), 1.23-1.20 (18H, m, *o*,*p*-CH (CH_3)$_2$); δc (100 MHz, $CDCl_3$) 150.60 (C), 150.42 (2C), 134.89 (C), 134.85 (C), 132.92 (C), 131.02 (CH), 129.85 (CH), 129.75 (CH), 129.51 (CH), 123.13 (2CH), 92.86 (C), 90.40 (CH), 89.49 (CH), 82.50 (CH), 78.87 (CH), 76.46 (CH), 58.03 (CH_2), 55.96 (CH_2), 48.07 (CH_2), 33.97 (CH), 29.02 (2CH), 25.47 ($2CH_3$), 24.81 ($2CH_3$), 23.66 ($2CH_3$); m/z ESI-MS $[M\text{-}Cl]^+$ 593.1.

N-[2-(4'-methoxy-1,1'-biphenyl-2-yl)methylamino]ethyl-2,4,6-triisopropyl-benzenesulfonamide.

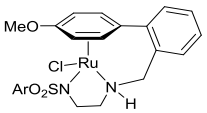


Ar = 2,4,6-(iPr)$_3$C$_6$H$_2$

To a mixture of *N*-2-(2,4,6-triisopropyl)benzenesulfonamido)ethylamine (0.500 g, 1.534 mmol, 1.10 eq) and MS 4A (0.6 g) in dry methanol (25 mL) was added 4'-methoxy-[1,1'-biphenyl]-2-carboxaldehyde (0.296 g, 1.395 mmol, 1.0 eq) followed by acetic acid (3-4 drops). The mixture was stirred at room temperature under an inert atmosphere for 4 h to form the imine. To this, $NaBH_3CN$ (0.351 g, 5.580 mmol, 4.0 eq) was added and resulting mixture was stirred at room temperature for 18 h. The reaction mixture was filtered and concentrated to give a residue. This was dissolved in DCM (60 mL) and washed with 1M NaOH (2 x 25 mL), dried over anhydrous Na_2SO_4, filtered and evaporated on a rotary evaporator to give the crude product. The crude compound was purified by flash column chromatography over silica gel using EtOAc: Pet. ether (6:4) to give the product as an oil. The compound solidified on standing overnight (0.728 g, 1.39 mmol, 99%). Mp 60-62 ^oC; HRMS found 523.2294 ($C_{31}H_{42}N_2O_3S$ H+ requires 523.2989, error = -0.7 ppm); ν_{max} 3291, 3244, 2961, 2929, 2834, 1610, 1600, 1459, 1445, 1164, 1098, 1072, 1016, 763, 706, 650 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.33-7.21 (6H, m, ArH), 7.14 (2H, s, *m*-C*H* of -$SO_2C_6H_2$-), 6.94 (2H, d, *J* 12.0, -ArH), 4.97 (1H, br s, -N*H*SO_2-), 4.19-4.05 (2H, m, *o*-C*H*(CH_3)$_2$), 3.85 (3H, s, -OCH_3), 3.66 (2H, s, -NHCH_2-biphenyl), 2.95-2.82 (3H, m, *p*-C*H* (CH_3)$_2$, -SO_2NHC$H_2$$CH_2$NH-), 2.60-2.57 (2H, m, -SO_2NHCH_2CH_2NH-), 1.28 (1H, s, -SO_2NHC$H_2$$CH_2$N*H*-), 1.25-1.2 (18H, m, *o*, *p*-CH (CH_3)$_2$); δc (75 MHz, $CDCl_3$) 158.77 (C), 152.53 (C), 150.28 (2C), 141.41 (C), 137.11 (C), 133.35 (C), 132.12 (C), 130.31 (CH), 129.88 (2CH), 129.06 (CH), 127.20 (CH), 127.09 (CH), 123.68 (2CH), 113.67

(2CH), 55.25 (OCH_3), 50.97 (CH_2), 47.36 (CH_2), 41.94 (CH_2), 34.08 (CH), 29.57 (2CH), 24.85 ($4CH_3$), 23.56 ($2CH_3$); m/z ESI-MS $[M+H]^+$ 523.2.

{*N*-[2-(4'-methoxy-1,1'-biphenyl-2-yl)methylamino]ethyl-2,4,6-triisopropylbenzenesulfonamide} ruthenium chloride **30.**



Ar = 2,4,6-$(iPr)_3C_6H_2$

N-[2-(4'-methoxy-1,1'-biphenyl-2-yl)methylamino]ethyl-2,4,6-triisopropylbenzene-sulfonamide (0.500 g, 0.958 mmol, 1.0 eq) and $[(C_6H_5CO_2Et)RuCl_2]_2$ (0.308 g, 0.479 mmol, 0.5 eq) were dissolved in dry DCM (50 mL) under N_2 and stirred at room temp for 30 min to give a brick red solution. The mixture was concentrated on a rotary evaporator to give dark orange residue. To this, chlorobenzene (150 mL) was added and the mixture heated at 140 ^oC for 2.5 h. The reaction mixture was cooled to room temperature and concentrated to give a dark brown residue. The solid was purified by column chromatography over Florisil using EtOAc:MeOH:Pet.Ether (60:1:39 to 60:5:35) to give a brown solid. The solid was recrystallized using mixture of MeOH and Et_2O to give pure complex **30** as an orange solid (0.064 g, 0.097 mmol, 10%). Mp decomposition >270 ^oC; HRMS found 623.1886 ($C_{31}H_{41}N_2O_3SRu$-Cl+ requires 623.1883, error = -1.3 ppm); ν_{max} 3197, 2952, 2858, 1598, 1537, 1461, 1441, 1249, 1230, 1041, 1018, 860, 804, 770, 652 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 7.53-7.41 (3H, m, ArH), 7.35-7.33 (1H, m, ArH), 7.04 (2H, s, *m*-C*H* of -$SO_2C_6H_2$-), 6.67 (1H, d, *J* 5.2,-C*H* of Ru-Ar), 5.82 (1H, d, *J* 5.2,-C*H* of Ru-Ar), 5.63 (1H, d, *J* 6.2,-C*H* of Ru-Ar), 5.35 (1H, d, *J* 6.2,-C*H* of Ru-Ar), 4.93 (1H, d, *J* 14.0, -NHC*H*H-biphenyl), 4.60 (1H, br d, -N*H*CH_2), 4.48-4.38 (2H, m, *o*-C*H* $(CH_3)_2$), 4.40-4.31 (1H, d, *J* 14.0, -N*H*CH*H*-biphenyl), 4.04 (3H, s, -OCH_3), 2.88-2.78 (1H, m, *p*-C*H* $(CH_3)_2$), 2.50 (2H, br d, -SO_2NHCH_2CH_2NH-), 2.33 (1H, br d, -SO_2NHCH_2C*H*HNH-), 1.95-1.85 (1H, m, -SO_2NHCH_2CH*H*NH-), 1.21 (6H, d, *J* 6.8, *p*-CH (C$H_3)_2$), 1.17 (6H, d, *J* 6.8, *o*-CH (C$H_3)_2$), 1.11 (6H, d, *J* 6.8, *o*-CH (C$H_3)_2$); δc (100 MHz, $CDCl_3$) 150.60 (C), 150.35 (2C), 134.83 (C), 134.51 (C), 131.86 (C), 131.53 (CH), 129.89 (CH), 129.66 (2CH), 127.36 (C), 123.15 (2CH), 86.13 (C), 82.33 (CH), 81.76 (CH), 75.34 (CH), 70.31 (CH), 56.82 (OCH_3), 56.59 (CH_2), 54.04 (CH_2), 47.83 (CH_2), 33.92 (CH), 28.77 (2CH), 25.51 ($2CH_3$), 24.65 ($2CH_3$), 23.62 ($2CH_3$); m/z ESI-MS $[M-Cl]^+$ 623.1.

Asymmetric hydrogenation procedures.

Asymmetric transfer hydrogenation in water: Catalyst (0.01 mmol) was placed in a Schlenk tube under an inert atmosphere followed by HCOONa (0.340g, 5.0 mmol) and H_2O (1 mL). The mixture was degassed three times and to this solution ketone (1mmol) was added followed by degassing 2 times. The mixture was stirred at 60 ^oC. The reaction was monitored by chiral GC. For chiral GC analysis, the sample from the reaction mixture was diluted with Et_2O and H_2O. The organic layer was separated, filtered through a short column of silica using hexane: EtOAc (1:1). The filtrate was analysed by chiral GC. After completion of the reaction, the reaction mixture was diluted with H_2O and extracted with Et_2O (2x5 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated to give crude compound. The crude compound was purified by flash column chromatography to give pure product.

Asymmetric transfer hydrogenation in FA:TEA: To a mixture of catalyst (0.002 mmol) in FA:TEA (5:2) (1.0 mL) was added ketone (2.0 mmol) and the mixure was stirred at 60 ^oC for 24h under an inert atmosphere. The reaction was monitored by TLC. After 24h, the reaction mixture was diluted with EtOAc and sat. $NaHCO_3$ soln. The organic layer was separated, washed with H_2O, dried over anhydrous Na_2SO_4, filtered and concentrated to give a brown residue. The crude compound was analysed by ^{1}H-NMR to give the conversion.

Reduction of ketones with hydrogen gas: Illustration with acetophenone: acetophenone (100 mg, 0.83 mmol), catalyst (0.01 eq. / 1 mol%), and iPrOH (0.5 mL) were added to a small test tube containing a stirrer bar. A solution of K_2CO_3 (5.8 mg, 0.042 mmol) in water (0.2 mL), or TMAO (1 mol%) was added, then the test tube was sealed in a Parr hydrogenator and charged with hydrogen to 30 bar, venting once. The sealed vessel was heated to the temperature indicated and stirred for the time given in the table. At the end of this time, the reaction was allowed to cool to rt, the pressure was carefully released and the sample was worked up and analyzed as previously described.

Data for the reduction products:

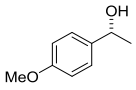
(*R*)-1-Phenylethanol**.**

This compound was prepared by the general procedure for ketone reduction using acetophenone (73 mg, 0.61 mmol), catalyst (*R*,*R*)-**14** (4.0 mg, 0.005 mmol) and FA/TEA (0.5 mL). Following solvent removal, the product was isolated as a colourless oil (50mg, 0.41 mmol, 68% yield, conversion >99%). $[\alpha]^D$ = +47.4 (c=0.50, $CHCl_3$), 97% ee (*R*), (lit[18] $[\alpha]^D$ = +45.3 (c 1.00, $CHCl_3$) 98% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.21 - 7.54 (5 H, m, ArH), 4.88 (1 H, q, *J* 6.4, C*H*OH), 1.97 (1 H, s, O*H*), 1.49 (3 H, d, *J* 6.5, CH_3); δ_C (101 MHz, $CDCl_3$): 145.82, 128.52, 128.33, 127.49, 125.39, 77.35, 77.03, 76.71, 70.45, 25.17. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=110°C, P = 18 psi, FID = 220 °C, inj = 220 °C), ketone 11.8 min, *R* isomer 17.6 min, *S* isomer 19.3 min.

(*R*)-1-(2-Methoxyphenyl)ethanol.

This compound was prepared by the general procedure for ketone reduction using *o*-methoxyacetophenone **31** (73 mg, 0.49 mmol), catalyst (*R,R)*-**14** (4.0 mg, 0.005 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (48 mg, 0.31 mmol, 65% yield, conversion 97%). $[\alpha]^D$ = +16.4 (c=0.39, $CHCl_3$), 87% ee (*R*), (lit[18] $[\alpha]^D$ = +16.0 (c 1.00, $CHCl_3$) 65% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.11 - 7.48 (2 H, m, ArH), 6.75 - 7.08 (2 H, m, ArH), 4.97 - 5.22 (1 H, m, C*H*OH), 3.86 (3 H, s, OCH_3), 2.52 - 2.71 (1 H, m, OH), 1.51 (3 H, d, *J* 6.6, CH_3); δ_C (101 MHz, $CDCl_3$): 156.52, 133.70, 133.56, 130.39, 128.27, 126.09, 120.81, 120.57, 111.60, 110.43, 77.44, 77.13, 76.80, 66.38, 55.49, 55.26, 31.84, 22.95. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=130°C, P = 18 psi, FID = 220 °C, inj = 250 °C), ketone 19.2 min, *S* isomer 23.7 min, *R* isomer 24.3 min.

(*R*)-1-(4-Methoxyphenyl)ethanol.

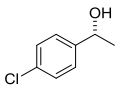


This compound was prepared by the general procedure for ketone reduction using *p*-methoxyacetophenone **32** (76 mg, 0.50 mmol), catalyst (*R*,*R*)-**14** (4.0 mg, 0.005 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (55 mg, 0.36 mmol, 72% yield, 94% conversion). $[\alpha]^D$ = +58.3 (c=0.53, $CHCl_3$), 96% ee (*R*), (li[19] $[\alpha]^D$ = +56.8 (c 1.00, $CHCl_3$) 95% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.28 - 7.35 (2 H, m, ArH), 6.84 - 6.95 (2 H, m, ArH), 4.87 (1 H, dd, *J* 6.4, 2.6, C*H*OH), 3.82 (3 H, s, OCH_3), 1.79 (1 H, br. s, OH), 1.49 (3 H, d, *J* 6.6, CH_3); δ_C (101 MHz, $CDCl_3$): 158.79, 138.01, 130.51, 126.56, 113.68, 113.58, 77.32, 76.68, 69.73, 55.33, 55.14, 26.18, 24.92. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=130°C, P = 18 psi, FID = 220 °C, inj = 250 °C), ketone 28.7 min, *R* isomer 29.6 min, *S* isomer 31.0 min.

(*R*)-1-(2-Chlorophenyl)ethanol.

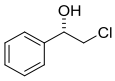
This compound was prepared by the general procedure for ketone reduction using *o*-chloroacetophenone **33** (98 mg, 0.63 mmol), catalyst (*R*,*R*)-**14** (3.8 mg, 0.0025 mmol), and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (60 mg, 0.38 mmol, 61% yield, >99% conversion). $[\alpha]^D$ = +64.8 (c=0.42, $CHCl_3$), 88% ee (*R*), (lit[18] $[\alpha]^D$ = +68.0 (c 1.00, $CHCl_3$) 98% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.58 (1 H, d, *J* 7.7, ArH), 7.31 (2 H, t, *J* 7.8, ArH), 7.19 (1 H, td, *J* 7.6, 1.5, ArH), 5.27 (1 H, q, *J* 5.8, C*H*OH), 2.48 (1 H, br. s., OH), 1.48 (3 H, d, *J* 6.5, CH_3); δ_C (101 MHz, $CDCl_3$): 143.03, 131.53, 129.30, 128.30, 127.13, 126.35, 77.32, 76.68, 66.83, 23.44. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=140°C, P = 18 psi, FID = 250 °C, inj = 220 °C), ketone 9.0 min, *R* isomer 14.9 min, *S* isomer 16.9 min.

(*R*)-1-(4-Chlorophenyl)ethanol.



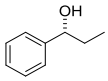
This compound was prepared by the general procedure for ketone reduction using 4'-chloroacetophenone **34** (83 mg, 0.54 mmol), catalyst (*R*,*R*)-**14** (4.1 mg, 0.005 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (53 mg, 0.34 mmol, 63% yield, 99% conversion). $[\alpha]^{D}$ = +51.7 (c=0.23, $CHCl_3$), 94% ee (*R*), (lit[20] $[\alpha]^{D}$ = +56.4 (c 1.00, $CHCl_3$) 95% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.21 - 7.40 (4 H, m, ArH), 4.87 (1 H, q, *J* 6.5, C*H*OH), 2.07 (1 H, br. s., OH), 1.47 (3 H, d, *J* 6.5, CH_3); δ_C (101 MHz, $CDCl_3$): 144.20, 133.02, 128.56, 126.76, 77.32, 76.68, 69.69, 25.21. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=130°C, P = 18 psi, FID = 250 °C, inj = 220 °C), ketone 15.6 min, *R* isomer 25.9 min, *S* isomer 28.7 min.

(*S*)-2-Chloro-1-phenylethanol.



This compound was prepared by the general procedure for ketone reduction using 2-chloroacetophenone **35** (77 mg, 0.50 mmol), catalyst (*R*,*R*)-**14** (4.1 mg, 0.005 mmol), and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (46 mg, 0.29 mmol, 59% yield, >99% conversion). $[\alpha]^{D}$ = +89.5 (c=0.31, $CHCl_3$), 97% ee (*S*), (lit[1f] $[\alpha]^{D}$ = +61.8 (c 1.00, $CHCl_3$) 96% ee (*S*)); δ_H (300 MHz, $CDCl_3$): 7.30 - 7.49 (5 H, m, ArH), 4.92 (1 H, dt, *J* 8.8, 3.3, C*H*OH), 3.76 (1 H, dd, *J* 11.2, 3.4, CH_2Cl), 3.66 (1 H, dd, *J* 11.2, 8.8, CH_2Cl), 2.62 - 2.73 (1 H, m, OH); δ_C (101 MHz, $CDCl_3$): 139.88, 129.73, 129.24, 128.65, 128.45, 126.12, 126.03, 77.32, 76.68, 74.05, 50.90. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=130°C, P = 18 psi, FID = 250 °C, inj = 220 °C), ketone 24.2 min, *S* isomer 29.9 min, *R* isomer 32.0 min.

(*R*)-1-Phenylpropanol.



This compound was prepared by the general procedure for ketone reduction using propiophenone **36** (69 mg, 0.52 mmol), catalyst (*R,R)*-**14** (4.0 mg, 0.005 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (36 mg, 0.26 mmol, 51% yield, 99% conversion). $[\alpha]^D$ = +69.7 (c=0.39, $CHCl_3$), 94% ee (*R*), (lit[1f] $[\alpha]^D$ = +53.6 (c 0.75, $CHCl_3$) 98% ee (*R*)); δ_H (400 MHz, $CDCl_3$): 7.22 - 7.38 (5 H, m, ArH), 4.58 (1 H, t, *J* 6.4, ArC*H*OH), 1.91 (1 H, br. s., OH), 1.68 - 1.88 (2 H, m, CH_2), 0.91 (3 H, t, *J* 7.5, CH_3); δ_C (101 MHz, $CDCl_3$): 144.57, 128.37, 127.47, 125.94, 77.32, 76.68, 76.00, 31.86, 10.11. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=130°C, P = 18 psi, FID = 250 °C, inj = 220 °C), ketone 30.7 min, *R* isomer 61.7 min, *S* isomer 66.2 min.

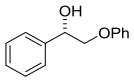
(*R*)-1-(Furan-2-yl)ethanol.

This compound was prepared by the general procedure for ketone reduction using 2-acetylfuran **37** (118 mg, 1.08 mmol), catalyst (*R,R*)-**14** (8.1 mg, 0.010 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (78 mg, 0.70 mmol, 65% yield, 99% conversion). $[\alpha]^D$ = +24.7 (c=0.36, $CHCl_3$), 94% ee (*R*), (lit[7] $[\alpha]^D$ = +24.9 (c 0.90, $CHCl_3$) 98% ee (*R*)); δ_H (400 MHz, $CDCl_3$): 7.33 - 7.43 (1 H, m, CH furyl), 6.34 (1 H, dd, *J* 3.2, 1.8, CH furyl), 6.24 (1 H, d, *J* 3.2, CH furyl), 4.80 - 4.95 (1 H, m, C*H*OH), 1.97 (1 H, br. s., OH), 1.55 (3 H, d, *J* 6.6, CH_3); δ_C (101 MHz, $CDCl_3$): 157.58, 141.91, 110.11, 105.09, 77.32, 76.68, 63.64, 21.26. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=75°C, P = 18 psi, FID = 250 °C, inj = 220 °C), ketone 16.3 min, *R* isomer 26.2 min, *S* isomer 28.0 min.

(*R*)-Cyclohexylethanol**.**

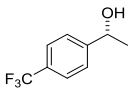
This compound was prepared by the general procedure for ketone reduction using cyclohexylmethyl ketone **38** (61 mg, 0.48 mmol), catalyst (*S*,*S*)-**15** (4.2 mg, 0.005 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (38 mg, 0.29 mmol, 60% yield, 97% conversion). $[\alpha]^D$ = -1.20 (c=0.57, $CHCl_3$), 71% ee (*R*), (lit[21] $[\alpha]^D$ = -3.01 (c 1.20, $CHCl_3$) 87% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 3.54 (1 H, quin, *J* 6.2, C*H*OH), 1.60 - 1.93 (6 H, m, Cy-CH_2), 1.54 (1 H, s, OH), 1.17 - 1.35 (3 H, m, Cy-CH_2 and Cy-CH), 1.15 (3 H, d, *J* 6.3, CH_3), 0.83 - 1.09 (2 H, m, Cy-CH_2); δ_C (75 MHz, $CDCl_3$): 77.43, 76.58, 72.15, 45.08, 28.65, 28.32, 26.47, 26.19, 26.10, 20.32. Enantiomeric excess was determined by conversion to the acetate derivative: (CP-CHIRASIL-DEX CB 50m x 0.25mm x 0.25μm, gas: helium, T = 115 °C, P = 9 psi, det = FID 220 °C, inj = 220 °C) ketone 24.6 min, *S* isomer 39.3 min, *R* isomer 42.1 min.

(*S*)-1-Phenyl-2-phenoxyethanol.



This compound was prepared by the general procedure for ketone reduction using α-OPh acetophenone **39** (425 mg, 2.0 mmol), catalyst (*R*,*R*)-**11** (3.5 mg, 0.005 mmol) and FA/TEA (1.0 mL). Following solvent removal the product was isolated as a white solid (323 mg, 1.51 mmol, 75% yield, conversion 100%). $[\alpha]^D$ = +56.6 (c=0.35, $CHCl_3$), 93% ee (*S*), (lit[5b] $[\alpha]^D$ = +58.8 (c 1.00, $CHCl_3$) 95% ee (*S*)); δ_H (300 MHz, $CDCl_3$): 7.51 – 7.32 (4 H, m, ArH), 7.37 – 7.22 (2 H, m, ArH), 7.03 – 6.87 (3H, m, ArH), 5.13 (1 H, d, *J* 9.1, C*H*(OH)), 4.17 – 4.06 (1 H, m, C*H*H), 4.01 (1 H, t, *J* 9.1, CH*H*), 2.78 (1 H, S, OH); δ_C (75 MHz, $CDCl_3$): 158.51, 139.76, 129.71, 128.72, 128.34, 126.43, 121.46, 114.78, 73.44, 72.75. Conversion and enantiomeric excess were determined by chiral HPLC analysis: (OD, eluent: hexanes/^{i}PrOH 90:10, detector: 250nm, flow rate: 0.7 mL/min) ketone 21.9 min, *R* isomer 18.0 min, *S* isomer 31.1 min. Ketone UV response is 12.35 times greater than for the alcohol.

(R)-(4-Trifluoromethylphenyl)ethanol.



This compound was prepared by the general procedure for ketone reduction using 4-trifluoromethyl acetophenone **40** (376 mg, 2.0 mmol), catalyst (*R*,*R*)-**11** (3.5 mg, 0.005 mmol) and FA/TEA (1.0 mL). Following solvent removal the product was isolated as a colourless oil (300 mg, 1.58 mmol, 79% yield, conversion 100%). $[\alpha]^{D}$ = +28.2 (c=0.84, $CHCl_3$), 95% ee (*R*), (lit[22] $[\alpha]^{D}$ = +29.3 (c 1.00, $CHCl_3$) >99% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.60 (2 H, d, *J* 8.0, ArH), 7.47 (2 H, d, *J* 8.0, ArH), 4.94 (1 H, q, *J* 6.6, C*H*(OH)), 2.12 (1 H, s, OH), 1.49 (3 H, d, *J* 6.6, CH_3); δ_C (101 MHz, $CDCl_3$): 149.83, 129.92, 129.60, 125.78 , 125.57 (q, *J* 3.8), 69.95, 25.50. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: hydrogen, T=120°C, P = 15 psi, FID = 250 °C, inj = 220 °C), ketone 7.3 min, *R* isomer 15.0 min, *S* isomer 16.63 min.

(R)-Tetralol.

This compound was prepared by the general procedure for ketone reduction using α-tetralone **41** (146 mg, 1.0 mmol), catalyst (*R*,*R*)-**11** (1.7 mg, 0.0025 mmol) and FA/TEA (0.5mL). Following solvent removal the product was isolated as a colourless oil (127 mg, 0.86 mmol, 86% yield, conversion 100%). $[\alpha]^{D}$ = -34.4 (c=0.57, $CHCl_3$), 99% ee (*R*), (lit[23] $[\alpha]^{D}$ = -32.3 (c 1.00, $CHCl_3$) 98% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.46 – 7.40 (1 H, m, ArH), 7.24 – 7.26 (2 H, m, ArH), 7.15 – 7.06 (1 H, m, ArH), 4.78 (1 H, d, *J* 5.1, C*H*(OH)), 2.91 – 2. 64 (2 H, m, CH_2), 2.05 – 1.86 (2 H, m, CH_2), 1.92 – 1.69 (2 H, m, CH_2); δ_C (75 MHz, $CDCl_3$): 138.93, 137.24, 129.14, 128.77, 127.71, 126.30, 68.29, 32.41, 29.38, 18.93. Conversion and enantiomeric excess were determined by chiral GC analysis: (CROMPAC CYCLODEXTRIN- β-236M-19, 50m × 0.25mm × 0.25µm, gas: helium, T=125°C, P = 15 psi, FID = 250 °C, inj = 220 °C), ketone 67.9 min, R isomer 81.9 min, S isomer 84.3 min.

(R)-Chroman-4-ol.

This compound was prepared by the general procedure for ketone reduction using 4-chromanone **42** (148 mg, 1.0 mmol), catalyst (*R*,*R*)-**11** (1.7 mg, 0.0025 mmol) and FA/TEA (0.5 mL). Following solvent removal the product was isolated as a colourless oil (117 mg, 0.78 mmol, 78% yield, conversion 100%). $[\alpha]^{D}$ = +64.63 (c=0.55, $CHCl_3$), 99% ee (*R*), (lit[24] $[\alpha]^{D}$ = +60.1 (c 0.20, $CHCl_3$) 96% ee (*R*)); δ_H (300 MHz, $CDCl_3$): 7.35 – 7.15 (2 H, m, Ar*H*), 6.98 – 6.79 (2 H, m, Ar*H*), 4.78 (1 H, d, *J* 4.6, C*H*OH), 4.26 (2 H, d, *J* 9.4, CH_2), 2.21 – 1.95 (2 H, m, CH_2), 1.92 (1 H, d, *J* 4.6, O*H*); δ_C (75 MHz, $CDCl_3$): 154.71, 129.85, 124.44, 120.72, 117.21, 63.38, 62.05, 30.95. Conversion and enantiomeric excess were determined by chiral HPLC analysis: (IB, eluent: hexanes/^{i}PrOH 95:5, detector: 250nm, flow rate: 1.0 mL/min), ketone 6.7 min, R isomer 9.0 min, S isomer 9.9 min. Ketone response is 20.12 times greater than for the alcohol.

Supporting information. ^{1}H and ^{13}C-NMR spectra of new ligands and complexes, chiral GC and HPLC of reduction products and X-ray crystallographic data for (*R*,*R*)-**11** and **29 (**CCDC 1571334 and 1571335). The Supporting Information is available free of charge on the ACS Publications website at DOI: **TBA**.

Conflicts of Interest. The authors declare no competing financial interests.

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